

CLASSIC REPRINT SERIES

THE TREATMENT OF MALIGNANT
INOPERABLE TUMORS WITH THE
MIXED TOXINS OF ERYSIPELAS
AND BACILLUS PRODIGIOSUS

With a Brief Report of 80 Cases Successfully
Treated With the Toxins From 1893 to 1914




by
William B. Coley

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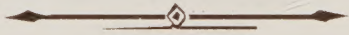
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*1st International Conference of Cancer
Brussels Aug 1917*

The treatment

of

Malignant inoperable tumors

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**mixed toxins of erysipelas and bacillus
prodigiosus**

**With a brief report of 80 cases successfully treated
with the toxins from 1893 to 1914,**

by WILLIAM B. COLEY, M. D., New York,

Professor of Clinical Surgery, Cornell University Medical School;

**Attending Surgeon to the General Memorial Hospital for the Treatment
of Cancer and Allied Diseases;**

Attending Surgeon to the Hospital for Ruptured and Crippled.

BRUSSELS

M. WEISSENBRUCH, PRINTER TO THE KING (LIMITED)

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1914



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*Read before the 3rd International Conference of Cancer Research Brussels,
August 1-5, 1913.*

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The treatment of malignant inoperable tumors with the mixed toxins of erysipelas and bacillus prodigiosus ⁽¹⁾. With a brief report of 80 cases successfully treated with the toxins from 1893 to 1914,

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The value of any method of treatment of cancer can be determined only after the lapse of a considerable period of time, after the disappearance of the tumor at least five years, and even a longer period if possible. My first paper upon the treatment of inoperable malignant tumors with living Cultures of the streptococcus of erysipelas was published in the *Amer. Journ. of Med. Sciences*, May, 1893. And the first paper upon the toxins of erysipelas and bacillus prodigiosus was published in July, 1894, in the *Amer. Journ. of Med. Sciences*. In various papers since that time, I have reported a steadily increasing number of successes varying little from 10 per cent of the total number treated. These results have already been duplicated and the value of the method confirmed by even a larger number of successful cases in the hands of other men. I believe that no more convincing evidence of the value of the method could be presented, than by making as careful and complete a report of these cases as is possible within the limits of time and space imposed by this Conference. Whoever is desirous of obtaining fuller details of these cases and of the early stages of the development of the method and the technique of

(1) Read before the 3rd International Conference of Cancer Research Brussels, August 1-5, 1913.

preparing the toxins, is referred to my earlier papers, the references to which will be found in the bibliography appended to this paper. A brief resume of some of the more important points brought out in previous papers, will be given here. In my paper read before the Royal Society of Medecine in London in 1909, I stated.

« I wish to emphasize the point that the method rests upon a solid foundation of accepted and indisputable clinical facts — namely, that in a considerable number of cases of inoperable cancer of all varieties, and especially sarcoma, such tumours have been known entirely to disappear under attacks of accidental erysipelas, and patients have remained well for many years thereafter.

« For those who refuse to accept clinical results unless confirmed by laboratory experiments, these latter tests have now been supplied, since, seven years ago Dr. MARTHA TRACY and Dr. S. P. BEEDE, of the Huntington Cancer Research Fund, showed that large multiple sarcomas in dogs rapidly disappear under both local and systemic injections with the mixed toxins of erysipelas and *Bacillus prodigiosus*. It is to note these. »

My attention was first called to the curative effect of accidental erysipelas in inoperable sarcoma by a certain case observed in 1891. In my studies of sarcoma at that time I made a careful analysis of all the cases of sarcoma (90 in number) operated upon at the New York Hospital during the preceding fifteen years. Among these cases was one of a small round-celled sarcoma of the neck, four times recurrent. At the fifth operation, in 1884, Dr. BULL found the tumour to involve the deep structures so extensively that it was impossible to remove it, and he gave up the attempt. The case was regarded as absolutely hopeless, when, shortly after the operation, the man developed a very severe attack of accidental erysipelas in the face and neck, followed two weeks later by a second attack. Within a few days after the beginning of the first attack the tumour began to soften and decrease rapidly in size. The history stated that when the patient left the hospital his tumours had entirely disappeared. There was no after-record of the case, but I made an effort to trace the patient, and finally found him alive and well, with no evidence of any local or general recurrence in the spring of 1891, seven years later. He was examined both by Dr. BULL and myself.

At this time I had not read of the experiments of Fehleisen

who had some years before attempted to inoculate seven patients suffering from inoperable malignant tumors with the living streptococcus of erysipelas which he had recently discovered, but I was so much impressed with the remarkable result of the case I have related, that I determined to try the inoculation of the living streptococcus of erysipelas as soon as I could find a suitable case. Very shortly, through the kindness of Dr. BULL, such a patient came under my care and was willing to assume the risks of the inoculation.

CASE 1. — A twice recurrent inoperable sarcoma of the neck with large secondary sarcoma of tonsil; treated with repeated injections of living cultures of erysipelas for four months; well eight years after treatment.

Mr. Z., 35 years of age. The patient had been operated upon twice by Prof. DURANTE of Rome, and last by Dr. W. T. BULL at the New York Hospital in March 1891. The tumor of the neck was so large that only a portion could be removed, and the general condition of the patient when I began treatment, May 4, 1891, was so bad that he was expected to live but a short time. The tonsillar tumor was so large that it was impossible for him to swallow solid food, and liquid food was taken with difficulty. From May 4 to October, 1891, I treated the patient with repeated local injections of living bouillon-cultures of the streptococcus of erysipelas. No attack of erysipelas occurred until October, yet improvement followed the injections, and whenever they were discontinued the growth increased in size. On October 8th, a severe attack of erysipelas followed the injection of a new and more virulent culture. During this attack the tumor of the neck nearly disappeared, the tumor of the tonsil decreased in size, and the general condition of the patient rapidly improved until he had regained his usual general health and strength. No further treatment was administered. He was repeatedly examined by myself and other surgeons. At the time of last examination, in September, 1895, there was a small mass at the site of the old scars upon the neck, apparently made up of cicatricial and fibrous tissue. This had remained unchanged for four years. The tumor of the tonsil was still present, though it had apparently shrunken some in size, and the features of malignancy must have been either entirely lost or held in complete abeyance. The general condition was excellent.

(Copy from records. New York Hospital Laboratory.)

Specimen No. 1870. *Microscopical examination and report* : « Operatiou, a piece of tumor about the size of an orange was removed, but a portion yet remains, being too deeply seated for extermination.

« Microscopically the tumor is composed of fibrous tissue and spindle-cells, the fibrous tissue predominating in placet and in others the spindle-cells.

« There are many areas of cells resembling mucous cells, and to be differentiated from myxomata; vascular supply abundant and vessel walls-formed by tumor-tissue.

« Diagnosis, *myxosarcoma*. » — Dr. FARQUHAR FERGUSON, pathologist to the New York Hospital.

The patient later returned to italy and remained in good health until eight years afterward, when he had a local recurrence which proved fatal. The fact that the tumor nearly disappeared during the administration of the living cultures of the streptococcus of erysipelas and following an attack of erysipelas and that the patient remained well for so long a period as eight years would seem the strongest possible evidence of the inhibitory action of the streptococcus. Furthermore, death from local recurrence established beyond any doubt the diagnosis of a malignant growth.

CASE 2. — *Large recurrent sarcoma of the back and groin; entire disappearance of both tumors; under injections of the living cultures of the streptococcus of erysipelas patient in good health without recurrence three yeards after the cessation of treatment. Death from abdominal metastasis a year later.*

G. K., male, aged 40 years; sarcoma of the back (lower lumbar region) 7×4 inches, with a secondary tumor the size of a goose-egg in the groin. The groin-tumor had been removed in January, 1892, but rapidly recurred. The patient was examined by Dr. WILLIAM T. BULL, who regarded the case as an inoperable sarcoma (fig. 3). The same diagnosis was made by a number of other surgeons. A section was removed under cocaine and examined by Dr. FARQUHAR FERGUSON, pathologist to the New York Hopital, who confirmed the diagnosis. The treatment with the living cultures of erysipelas was

begun in the erysipelas wards of Bellevue Hospital in April, 1892, and daily local injections were given for two weeks before an attack of erysipelas was produced. The attack was very severe, but during the same both tumors rapidly decreased in size and entirely disappeared within a few days there after. Recurrence followed in July, and both tumors grew more rapidly than before. The injections were resumed, and between October, 1892, and January 1, 1893, he had four additional attacks of erysipelas, but mild in character.

In December, 1892, he was exhibited before the Surgical Section of the New York Academy of Medicine. The influence upon the tumors was striking, but less marked and more temporary than the first attack. In January, 1893, I removed the recurrent tumor of the back but left the groin undisturbed. After three weeks there was a recurrence in the back, and I began using the toxic products of erysipelas and bacillus prodigiosus injecting them locally in the back and groin-tumor. This preparation was the one made by filtering the bouillon cultures through porcelain.

The tumors quickly disappeared. The injections were discontinued in March, 1893, and the patient remained entirely well for over three years and then had a recurrence in the abdomen, involving the liver, which progressed very rapidly, with fatal issue three and a half years after the disappearance of the original tumor.

(Copy from records, New York Hospital Laboratory.)

Pathological report : « The tumor (fig. 4) is a sarcoma, in which the cells are round, oval, and spindle, in which everywhere there is seen a stroma of fibrous tissue, apparently the remains of the subcutaneous tissue which has not been completely destroyed during the development of the tumor. Yellow elastic fibres are quite abundant throughout the tumor, but the vascular supply is not very abundant. » — Dr. FARQUHAR FERGUSON, pathologist to the New York Hospital.

Effect of accidental erysipelas upon malignant tumors.

First, a further word upon the clinical observations of accidental erysipelas in inoperable tumors. In one of my earlier papers, *Amer. Journal of Medical Sciences*, 1893 : « The treatment of malignant tumours by repeated inoculation of the living germ of erysipelas ». I collected thirty-eight cases of malignant tumors (sarcoma and car-

cinoma) in which an attack of erysipelas had occurred, either by accident or by inoculation. In twenty-three cases the attack was accidental, and in fifteen the result of inoculation. Seventeen were sarcoma, seventeen carcinoma, and in four cases the type of tumour was not stated. Of the seventeen cases of carcinoma, three were permanently cured. One, a probable carcinoma, was well five years after the attack of erysipelas. The remaining thirteen showed more or less temporary improvement. Of the seventeen cases of sarcoma, seven were well from one to seven years afterwards. In the remaining ten cases, nearly all showed improvement, some disappearing entirely and later recurring.

In the *American Journal of Medical Sciences*, 1906. I published six other cases of cancer — five epithelioma and one sarcoma — in which an attack of erysipelas had intervened in the course of the disease :

- (1) Recurrent cancer of the breast. Patient well nine years;
- (2) Sarcoma of the neck (entire disappearance). Patient well eight years;
- (3) Epithelioma of the face, eighteen years' duration (entire disappearance). Local recurrence several years later. Again disappeared under one month's treatment with the toxins. Probable recurrence six months later;
- (4) Epithelioma of the face, lip, and nose. Disappeared under very severe attack of erysipelas. Patient well two years later, when he died of another trouble;
- (5) Epithelioma of the face of two years' duration. Entire disappearance under attack of erysipelas. Patient well at last observation, six months later;
- (6) Epithelioma of nose. Eight years' duration. Entire disappearance under attack of erysipelas. Patient well several years later.

Eschweiller, in a monograph published some years after my earlier report, made a very complete study of accidental erysipelas associated with malignant tumors, and collected sixty-nine cases from the literature, twenty-seven of which were sarcoma, thirty-eight carcinoma, and five in which the type was undetermined. Of the sarcoma cases, seven showed temporary improvement, the tumor entirely disappeared in ten, and in one case the disease disappeared but later

recurred; there were nine apparent cures, and four patients were well from two to eight years.

In the thirty-eight carcinoma cases, twelve showed temporary improvement, in eight the tumor entirely disappeared, in three cases recurrence followed disappearance; there was no apparent effect in nine cases, and in six, the patient died of an attack of erysipelas.

Of the thirty-eight cases of carcinoma, nineteen occurred in the breast.

During the year 1891 through the generosity of Mr. ARCHER M. HUNTINGTON, and Mrs. COLLIS P. HUNTINGTON, the founder of the Huntington Fund for Cancer Research, of the General Memorial Hospital, and the generous and invaluable aid of Prof. WILLIAM T. BULL, a special pavilion was erected on the Grounds of the New York Cancer Hospital (now the General Memorial Hospital for the treatment of cancer and allied diseases), in order that further experiments with the living cultures might be carried on. In the ten cases of inoperable cancer treated, cultures of pronounced virulence were used, and the injections were continued for a considerable time. However, it was these very cases, in which I had failed to produce erysipelas, that proved to be the most valuable, as they furnished a hint as to the best practical method of utilizing the antagonistic action of erysipelas without its dangers.

While some of the cases in which actual erysipelas was produced showed a most marked and rapid decrease in the size of the tumors (in two cases entire disappearance in two weeks), the cases in which repeated injections of bouillon cultures failed to produce erysipelas were attended with all the general symptoms of an attack of erysipelas *e. g.*, nausea, vomiting, headache, malaise, and high temperature, but always disappearing within twenty-four to forty-eight hours. The effect upon the tumors was unmistakable. In some cases there was necrobiosis and discharge, in others diminution by absorption without breaking down, and in almost every case there were signs of retrograde action. These changes were always much more marked in sarcoma than in carcinoma.

The great difficulty in producing erysipelas, the danger necessarily attending an attack of erysipelas (I myself having had two fatal cases from inoculation) added to the fact that marked improvement followed repeated injections of bouillon cultures, convinced me that a certain

portion, if not all, of the beneficial action was due to the toxic products of the streptococcus rather than to the germ itself.

My first experiments with the toxic products were made in 1892, with bouillon cultures treated by heat (58° F.). The reaction following injections of this fluid was similar in character to that caused by living cultures, but somewhat less severe. The effect upon the tumors was also slightly less marked, the destructive effect of heat upon most bacterial products being well known. I very soon began using filtered cultures prepared for me by Dr. ALEXANDER LAMBERT of New York. These injections produced only moderate reactions, and only slight inhibitory effect upon the tumors. I tried to increase the virulence of the streptococcus getting cultures from fatal cases when possible. At this time, early in 1893, I learned that ROGER of PASTEUR'S Institute had succeeded in intensifying the virulence of the streptococcus of erysipelas by growing with it the bacillus prodigiosus, and I adopted his idea though he had never used in on the human being, nor had he suggested its use as a therapeutic measure.

Injections of the toxic products of erysipelas, combined with small quantities of the products of the bacillus prodigiosus, were begun early in February, 1893, at the New York Cancer Hospital. They were given locally, directly into the tumor, and in slightly increasing doses. The reaction following the injections was severe, and corresponded exactly with that seen at the beginning of an attack of erysipelas. The chill usually occurred within the first half-hour after injection, though sometimes delayed an hour. Some local redness accompanied the reaction, but usually both local and constitutional signs had disappeared at the end of twenty-four hours.

The action of the combined toxins was much more powerful than that of erysipelas alone, and the effect upon the tumor much more marked. Case 2 which I have described was finally apparently cured by the toxins used in this way though internal metastasis occurred three-one-quarter years later.

Shortly after this I determined to utilize the toxins contained in the dead bacilli and streptococci as well as the soluble toxins as heretofore, and at the suggestion of Dr. B. H. BUXTON, of the Loonies Laboratory grew the germs together and then sterilized them by heat. Still more powerful reactions occurred this time after very small doses, M. $\frac{1}{2}$, and the action upon the tumors was likewise correspondingly

greater. This preparation was used until six years ago when Dr. MARTHA TAAEY, of the Huntington Cancer Research Fund, and the Cornell Medical School Laboratory introduced a modification, which for the first time it possible to accurately standardize the dosage.

The technique I have published in several previous papers, last in the paper read before the Royal Society of Medicine in London, July 1909. *London Practitioner*, 1909, and *Transaction of the Royal Society of Medicine*, 1909. As early as 1894 I had stated that the clinical results seemed to show that there was some inherent curative substance in the bacillus prodigiosus alone, aside from any effect it might have in increasing the virulence of the streptococcus of erysipelas and this opinion was afterwards confirmed by Dr. BREE and Dr. TAAEY who, in 1908, succeeded in curing sarcoma in dogs by the toxins of bacillus prodigiosus alone.

Indications for treatment :

(1) Inoperable sarcoma.

(2) Cases of operable sarcoma in which operation entails the sacrifice of limb or the loss of the lower jaw. Here the toxins are to be recommended for a limited period of two to three weeks in the hope of saving the limb. This happy result has now been obtained in some twenty cases (including the results of other men).

(3) After operation as a prophylactic against recurrence.

(4) Carcinoma. — The number of successful cases of inoperable carcinoma treated with toxins though still small, is sufficiently striking to justify the use of the toxins after all cases of primary operation, as a prophylactic against recurrence. These successes, while not sufficient at present to justify advocating the toxins in all cases of inoperable carcinoma, are sufficient to justify further investigations, as no other mode of treatment has, I believe effected even this small number of definite permanent results.

(5) In combination with incomplete operations, or with any other agents known to have a marked inhibitory action, *e. g.*, radium, or X-rays.

Theory of action of the toxins. — Until we have more definite knowledge of the causes of sarcoma and carcinoma, we cannot attempt to give any exact explanation of the action of the toxins. I have long

held the opinion that the exciting cause of malignant tumors, both sarcoma and carcinoma, was some extrinsic microbic organism. This theory has not been accepted by the majority of pathologists, yet during the past few years, much new evidence has been brought forward in its support, and some of its former opponents are now willing to admit that sarcoma is of microbic origin. If we admit that one variety of malignant tumor, sarcoma is of germ origin, the probability is strong that the numerous other varieties, epithelioma, endothelioma, carcinoma, are likewise of similar origin, for the most experienced pathologists often differ among themselves in the classification of the various types of malignant tumors. They may not be, and probably are not all due to the same specific micro-organism, but to different species of organisms, more or less closely related. If we assume sarcoma to be of germ origin, the explanation of the action of the toxins is not difficult.

*Changes noted following the injections
of the mixed toxins in inoperable sarcoma.*

The macroscopic as well as the microscopic changes observed by myself and others have been precisely the same as those formerly noted in cases of sarcoma treated by inoculation of the living germ. First, the tumour becomes much paler owing to decreased vascularity; second, it becomes much more movable and less fixed to the surrounding tissues, these changes being often noted after the first two or three injections; third, it soon begins to show areas of softening, due to caseous degeneration or necrobiosis of the tumour elements; fourth, gradual disappearance, either by absorption — which is more apt to be the case in the firmer tumours (e. g., spindle-cell or fibro-sarcoma) — or, in other cases (especially the round-celled and more, vascular varieties), by breaking down and liquefaction of the tumour-tissues. In such cases incision and drainage may be sometimes advisable, provided the tumours are in accessible regions.

These changes are precisely the same, whether the toxins have been injected directly into the tumour or whether the injections have been made in remote parts of the body, proving that the action of the toxins is systemic rather than local. In a certain number of cases — in my own experience in a little over 10 per cent — the degenerative pro-

cess has gone on until complete absorption of the tumours has taken place and the patients have remained cured. In other cases improvement is only temporary, and after a few weeks, in spite of continued injections and increased doses, the tumour again begins to show signs of growth and continues until a fatal issue. In a very few instances, especially in cases of very large and vascular tumours, particularly the melanotic type — which of late many pathologists are inclined to class as carcinoma, instead of sarcoma — no marked beneficial effects have been noted at any time.

Dose of the mixed and toxins up Erysipelas Bacillus prodigiosus. — It is safe to begin with M. $\frac{1}{4}$ to $\frac{1}{2}$ 0.15 to 0.03 c. c. (diluted with boiled water to insure accuracy of dose) in adults, preferably systemic at first (remote from the tumor) and increasing daily by M. $\frac{1}{2}$ until the desired reaction is obtained. The more rapidly the dose is increased and the more quickly a marked reaction is obtained, the greater the chances of success, but in most cases I believe it is unwise to increase faster than by M. $\frac{1}{2}$ = 0.03 c. c.

Systemic or local injections. — In the earlier cases the injections were nearly all local, but further experience, especially with intra-abdominal tumors, proved that the action was largely systemic and the results were nearly as good as in cases in which the injections were made directly into the tumors. In easily accessible tumors, I believe that the best results will be obtained by combining systemic with local injections, always beginning with systemic and remembering to start the local injections with the minimum dose, not over $\frac{1}{8}$ to $\frac{1}{4}$ of a minim. A more severe reaction will often be caused by a dose of M. $\frac{1}{4}$ into a vascular sarcoma, than five minims injected systemically (M. $\frac{1}{4}$ = 0.15 c. c.).

Locations of injections. — I prefer the pectoral region or buttocks. The pectoral regions for tumors of the upper half of the body, the buttocks for the lower half. Very much depends upon the judicious determination of the dose in the individual case. I had one very brilliant success in a case of recurrent inoperable spindlecelled sarcoma of the parotid with cervical metastasis, in which the same preparation of the toxins had been tried by another surgeon, and

pronounced a failure. I simply increased the dose until severe reactions with temperature of 103-103.5° F. occurred (which, being in fine physical condition he was quite well able to bear) and in two months his tumors had entirely disappeared and he lived for six years and died of an independent trouble (He received daily doses).

Some patients cannot stand such reactions and in every cases much judgment must be used in adapting the dose to the individual conditions.

In some cases I have obtained better results from daily injections of smaller doses. I have a feeling that the best results are obtained by pushing the dose to a good reaction as rapidly as is consistent with safety in the early days of the treatment.

Duration of treatment. — It is very hard to lay down definite rules as to how long the toxins should be given. My own feeling based on an experience of twenty years is that there is more danger of stopping too soon than in continuing the treatment too long. I believe that in several of the cases in which recurrence took place this might not have occurred had the toxins been given for a longer period. As evidence that long continued treatment results in no harm, I will cite one patient who had eight operation for spindle-celled sarcoma of the chest wall before the toxins were used. They were kept up with occasional intervals of rest for a period of four years. The treatment did not interfere with his professional work (he is a surgeon with a very large practice) and he is still in good health at present, nineteen years later.

In one successful case the injections were given for less than a month and the patient is now well seventeen years. In still another, the tumor (abdominal wall and pelvis) disappeared after thirty-one injections, and with but a single pronounced reaction. In one case of recurrent inoperable carcinoma of the breast and cervical glands, the injections were kept up with intervals of rest for two-and-a-half years. The later doses were small and only sufficient to produce a very slight rise in temperature, 99 and slight malaise the tumors entirely disappeared. This patient is still well five years later. I should say the average duration of treatment in the successful cases, has been about to three two-and-a-half months.

Duration of treatment when give for prophylaxis. — When given after primary or secondary operation in the hope of lessening the chances of a recurrence, it is unnecessary and unwise to give the larger doses that are indicated in dealing with inoperable tumors. I believe that small doses, just enough to give a slight reaction *e. g.*, temperature 99-100° F., two to three times a week, will be sufficient. It is important in such cases to continue the treatment with intervals of rest for a least six months. The treatment can easily and safely be carried out by the family physician, and this use of the toxins has already been adopted by many prominent surgeons. In some cases it is wise to continue the treatment much longer than six months.

In my opinion, based on personal experience, this is by far the most important and promising field for the toxins. If they are able to cause the destruction and absorption of very large inoperable tumors, in a very considerable number of cases, there is much more reason to believe that they will be able to destroy the few cells that are left behind after operation, and which form the starting point of the recurrence.

Dangers of the toxins. — The risks of the treatment have been unduly emphasized. While I have personally found the administration of the mixed toxins practically free from danger, there have been several fatal cases in the hands of other physicians brought to my notice which, taken together, show that there are certain risks connected with the treatment. If, however, the precautions which I have always carefully emphasized in former papers be observed, these risks, I believe, will be reduced to a minimum. Most of the fatal cases that have occurred have been due to a neglect of these precautions. In my own experience in nearly 700 cases there have been only three deaths.

In the majority of the fatal cases thus far observed death was apparently due to an embolism. This was the causes in two of my own cases, and in both instances the general condition of the patients was extremely bad; there was generalization of the disease and very marked involvement of the mediastinal glands. In both cases the patients had only very small doses of the toxins, which were not pushed to the point of giving any marked reactions.

Most of the deaths in the hands of other men have been due, I believe, to too large an initial dose given directly into a vascular primary growth. In recent years I no longer inject the initial dose directly into a tumour, but first test the individual susceptibility of the patient by systemic injections in the buttocks or pectoral region ; after a few such injections local treatment may be begun, always starting with a minimum dose. I rarely give more than $\frac{1}{8}$ mm. into the tumour in children, especially if situated in the neck or mediastinum, and never more than $\frac{1}{4}$ mm. in adults. I have seen a temperature of 103° F. result from $\frac{1}{5}$ mm. injected into a large cervical tumour in a child. In one of the fatal cases in the hands of other men death resulted from an injection of $\frac{1}{4}$ mm. of Dr TRACY'S early preparation (twice as strong as at present) directly into a mediastinal tumour. This was an elderly woman of very feeble vitality.

Diagnosis. — Every effort has been made to establish the correctness of the diagnosis in the cases reported.

A careful microscopical examination has been made in all but eight cases, and not merely by a single pathologist (the usual custom in reporting cases cured by surgical operation), but by a number of pathologists, and in many instances, confirmed by the highest authorities in pathology in America, including Prof's. WM. H. WELCH of JOHNS HOPKINS, T. MITCHELL PRUDDEN of Columbia, JAMES EWING of Cornell, W. F. WHITNEY of Harvard, E. K. DUNHAM of Carnegie Laboratory, and JOHN CAVEN of the University of Toronto.

The fact that the tumors in most instances were recurrent, and in all, inoperable, rendered the diagnosis practically certain without the aid of the microscope. One hypothesis often mentioned in explanation of the results in my earlier reports, was that of spontaneous *disappearance*. Were we dealing with a single case or with a very few isolated cases, such explanation might be worthy of consideration, but a careful study of the cases of malignant tumors in which the diagnosis was clearly established that have spontaneously disappeared and remained cured, show such cases to be extremely rare.

In discussing this point at a meeting of the Johns Hopkins Medical Society, April 6, 1896, at which time I had a comparatively small number of successes, Prof. WM. H. WELCH said :

I see no way of gainsaying the evidence which Dr. COLEY has brought

forward, that there is something specifically and genuinely curative in his method of treatment. A single undoubted cure of a demonstrated cancer or sarcoma by this treatment would be enough to say definitely that the treatment exerts some specifically curative influence, for the spontaneous disappearance of undoubtedly malignant growths of this character is almost unknown. Dr. COLEY, has, however, presented us positive proof not only of one, but of numerous cases of malignant tumor cured by his method.

As I have already stated in a previous paper, it would be somewhat remarkable that my cases should be thus far, practically the only ones with both clinical and microscopic diagnosis of malignancy, to disappear spontaneously; and it would be more remarkable still that this disappearance should be coincident with the beginning of the treatment with the toxins. Furthermore, it would be clearly unfair to rule out these cases on the ground of errors in diagnosis without ruling out the cases of cures following operations for sarcoma. Both have been subjected to the same standards of diagnosis, with this important difference, that the cases treated with the toxins have been subjected to far more severe diagnostic tests.

The chances of one man having upwards of eighty cases of spontaneous disappearance of inoperable malignant neoplasms, most of which were recurrent and many of them extremely far advanced and some with extensive metastases, and such disappearance coincident with the administration of the mixed toxins, would be so small that the supposition can scarcely be regarded seriously.

We are then forced to conclude that the toxins have a certain definite inhibitory action upon malignant tumors which varies greatly not only in different types of tumor but upon the same types in different individuals and under different and not clearly understood conditions.

A study of this group of cases in which the tumor entirely disappeared under the influence of the toxins and at some later period, varying from seven or eight, months to eight years, recurred, furnishes the most convincing proof of the inhibitory action of the toxins. These cases cannot possibly be explained away on the ground of errors in diagnosis. In many of these cases the results were most striking, take *e. g.*, the case of Z., No 4, a very large, recurrent

sarcoma of the neck and tonsil, so far advanced that the patient was emaciated and unable to swallow any but liquid food, the tumor completely disappeared under an attack of erysipelas artificially produced in 1891, the patient regained his normal health and remained well for eight years and then died from a local recurrence.

Another, even more remarkable case than the above, is that referred to me by Dr. A. G. GERSTER eight years ago, H. M. (case 3), with a very rapidly growing lymphosarcoma of the tonsil with extensive metastatic involvement of the glands of the neck. The tumor was recurrent and inoperable at the time. The primary and secondary tumors entirely disappeared under seven weeks' treatment with the mixed toxins, without any other treatment, systemic injections only being given. The patient completely regained his normal health and remained well for six years, then developed a similar tumor in the opposite tonsil with rapid involvement of the glands of the neck. The tumors promptly recurred after two subsequent operations and caused death in three months. The microscopical examination in this case was made by Dr. Jas. EWING, who pronounced it a round celled lymphosarcoma.

Another equally striking case, even more malignant, is that of an inoperable lymphosarcoma of the tonsil and neck, which entirely disappeared under the toxin treatment alone. Six months later, a local recurrence occurs which no longer is controlled by the toxins and causes death within six months. Autopsy in this case showed absolutely no other involvement.

I do not believe that in these cases, particularly, *e. g.* Case 3 we have true metastases from the original tumor, (in this case, the disease appeared in other tonsil after six years). but that we are dealing rather with an infectious disease of bacterial origin, an example of what Adami (*Journ. Am. Med. Ass.*, December, 23, 1899) describes as latent infection or subinfection. Adami shows that « not only lymph nodes, respiratory and of the alimentary tract of normal animals, constantly show cultures of bacteria, but also that properly prepared organs, like liver and kidneys yield culture of pathogenic and non-pathogenic bacteria and that through the leucocytes these bacteria were constantly carried into the system and constantly being destroyed in healthy animals. »

The action of the toxins, I believe, increases the bactericidal properties of the leucocytes which destroy the infectious microorganisms

that are the inciting cause of lymphosarcoma and probably of the other varieties of tumor as well. The cells of these tumors of lower vitality those the normal tissues, having been deprived of the proliferating and stimulating influence of the microorganisms, undergo necrobiosis and are either absorbed or to slough away.

In certain cases, unfortunately in the majority of cases this inhibitory influence is insufficient to completely arrest the growth of the malignant tumor.

Carcinoma.

The earlier clinical observations of cases of undoubted carcinoma, in which an attack of intercurrent erysipelas was immediately followed by great improvement in the local and general condition of the patient, and in some cases by complete disappearance, ending in a permanent cure, furnish convincing evidence that the streptococcus has a marked inhibitory action upon neoplasms even of the carcinomatous type.

Hence, in my first studies with the living cultures of erysipelas, and later with the mixed toxins of erysipelas and bacillus prodigiosus, I tried their effect upon both sarcoma and carcinoma. The results were so much more encouraging in sarcoma, that I temporarily abandoned my experiments in carcinoma, and limited my investigations practically to inoperable sarcoma. In some of my earlier cases of carcinoma, however, very remarkable results followed the use of the toxins. There was complete disappearance in three cases; apparent cure in two, one well six years later, when last observed.

After having established, I believe, the value of the toxins in inoperable sarcoma, and further, influenced by the very striking result in a case of recurrent inoperable carcinoma of the breast, treated with the toxins five years ago, by another surgeon under my direction, in which the tumor with metastases in the neck, entirely disappeared and the patient has remained well, I believe it advisable to make a further and more systematic study of selected cases of carcinoma treated with the toxins.

Melanotic sarcoma.

In my earliest papers I expressed the opinion that the melanotic type of tumor seemed least amenable of any to the influence of the toxins. My further experience has confirmed this view. Yet, as the following results show — chiefly in the hands of other men — even this class of cases should be given the benefit of a trial with the toxins before being abandoned as hopeless. Dr. HOWARD LILIENTHALS case, an extensive inoperable melanotic sarcoma of the chestwall, remains well ten years. The case of Dr. GREENWOOD, of Leeds, England, a recurrent melanotic sarcoma of the neck has remained well nearly two years after disappearing under the toxin treatment.

I believe that practically all the so-called « sarcomas », starting in pigmented moles, are really of epithelial origin. This explains why the results of the toxins in these case correspond more nearly to those obtained in carcinoma, than in sarcoma.

The following reports contain brief histories of my personal cases. The results of other men have been tabulated as space does not permit giving the histories in full.

I have tried to present the evidence contained in these cases in an impartial way. While in the great majority of cases the diagnoses have been confirmed by microscopical examination made by competent pathologists, some few cases which have not had such confirmation, and it might be asked why these were not left out. My reason for including them is, that the clinical evidence in most of these cases is so strong that little reasonable doubt can exist as to the correctness of the diagnosis of malignant tumor. The only doubt that might exist is as regards the exact type of tumor, and this uncertainty might still remain even after a microscopical examination, for not infrequently have I received reports from experienced pathologists stating their inability to tell whether a certain tumor is sarcoma, or endothelioma, or Hodgkins Disease, or even carcinoma; but they are willing to state positively that it is a malignant tumor of some sort. So, these cases have been included and it is left to the impartial critic to weigh the evidence therein contained, or to reject it altogether.

It is a noteworthy fact that seventeen of my successful cases were lymphosarcomas; primary in the tonsil in six cases with extensive involvement of the glands of the neck in all; primary in the neck in six cases; primary in the inguinal glands in three, in the axillary glands in two, in the mesenteric glands and intestine in one. FABIAN (*Münchener Medizin, Woch.*, Aug. 25, 1913).

The statement has been made on high authority that there are no cases on record of a cure of lymphosarcoma after more than single gland has become involved, either by surgery or the X-ray. This has been held as particularly true of lymphosarcoma of the neck and tonsil. Certainly, I have never seen a patient with lymphosarcoma cured by surgery, nor do I know of any lasting cures with the patient well over three years treated, either by surgery or X-ray. This fact makes all the more remarkable the results from the toxin treatment in the following group of cases of lymphosarcoma, ten of which remained well over three years, one recurred after three years, one after six years and one after one-and-a-half year.

The tables of other mens cases show a total of 102 cases observed from 1-20 years treated with the mixed toxins by other men. Of these :

4	remained well from	15-20 years
8	—	— —	10-15 years
19	—	— —	5-10 years
32	—	— —	3-5 years

making 63 well over three years.

19	have remained well from	2-3 years
20	—	— — —	1-2 years
3	—	— — —	less than 8 months

In twelve a recurrence took place at intervals varying from a few months to four years after the disappearance of the disease under the toxin treatment.

Seventeen of the cases were lymphosarcomas, eight of which remained well over three years; in one there was a recurrence after four years, in three others after six months.

SERIES OF CASES OF LIMPHO SARCOMA.

CASE 3. — *Small round-celled sarcoma of the neck and tonsil. Entire disappearance in seven weeks under treatment with the mixed toxins of erysipelas and bacillus prodigiosus; recurrence in other tonsil and other side of neck seven years later. Very rapid growth death in form months.*

H. M., 32 years. The patient was referred to me on October 17, 1905, by Dr. ARPAD G. GERSTER, of New York, as on inoperable sarcoma for toxin treatment with a history of having noticed a



Fig. 1 (Case 3).

swelling on the left side of the neck, just behind the sternomastoid muscle, in about the middle of August, 1905. At about the same time he also noticed an enlargement of his left tonsil; there was no pain at first, but as both tumors increased rapidly in size, they soon

became painful. In the latter part of August, 1905, the patient was operated upon at St. Mark's Hospital by Dr. CARL BECK, who made an attempt to remove the tonsil tumor, as well as that of the neck; he found it impossible, however, to make complete excision. X-ray as well as radium treatment were tried with little or no effect. On October 13, while under the care of Dr. GOLDWATER, at the New York Polyclinic, a portion of the tonsil tumor was removed and examined by Dr. F. M. JEFFRIES, director of the Pathological Laboratory of the New York Polyclinic, and also by the Pathologist of the Practitioners, Laboratory, both of whom reported the tumor to be a small round-celled sarcoma (see pathological reports below). I first saw the patient October, 17, 1905 and found the left side of the neck occupied by a soft globular tumor, about the size of half an orange; it extended from the angle of the jaw in front to the mastoid process behind and downwards nearly to the clavicle. Examination of the left tonsil showed it enlarged to two to three times its normal size. The patient's general health had been but little affected. He was admitted to the General Memorial Hospital in October, 17, 1906 and immediately put upon the mixed toxins of erysipelas and bacillus prodigiosus without any other treatment. Daily injections were given, alternating one day into the tumor direct, the other, into the pectoral region. The highest dose given was seven minims; his temperature ranged between 99.5°, and 103°. In less than a week there was decided decrease in the size of the tumor and increase in mobility. The diminution continued steadily until, at the end of six weeks, both the servical and tonsil tumor had apparently entirely disappeared. The patient left the hospital at the end of seven weeks. The toxins were, however continued twice a week for some time, as a prophylactic against recurrence. He remained in good health up to the fall of 1911, and had been shown before various Medical Society meetings. At this time there was a recurrence in the tonsil and neck, which was removed by Dr. ERDMAN, December, 1911. Unfortunately the specimen was lost. The growth returned very rapidly, and in less than three weeks had become larger than at the time of the last operation. In January 15, 1912, the patient entered my service at the General Memorial Hospital where a very extensive operation was performed by Dr. WM. A. DOWNES and myself, mass about the size of an organ and several smaller masses around

the clavicle, as well as the entire sterno-mastoid muscle. This tumor was carefully examined by Dr. EWING, who pronounced it round-celled sarcoma. The patient made a good recovery, but refused to remain at the hospital for the toxin treatment, as I had advised. The latter was, therefore, carried out for a few weeks by his family physician, when the patient lost hope, and declined further treatment. The tumor grew with marked rapidity causing death within less than two months after the last operation.

Pathological reports :

October, 17, 1905.

« The neoplasm submitted has the character of round-celled sarcoma. The cells are a mixture of small and large. The tumor appears decidedly malignant, and has probably extended beyond local limits. Examination shows that the cells have invaded the blood vessels, and could easily have been swept into the current. »

(Signed) *Practitioners Laboratory.*

December, 21, 1911.

« Specimen consists of a mass of tissue removed from the tonsil.

« Microscopical examination shows the following changes :

« The tissue is irregularly covered externally by stratified squamous epithelium. The main volume of the tissue is made up of round cells, the nuclei of which show mitotic figures. These cells are closely packed together and show no attempt to reproduce the lymphoid follicles normally encountered in the tonsil. The cellular foci are definitely surrounded by connective tissue.

« The diagnosis in this case rests between a sarcoma of the tonsil and a granuloma. From the histological appearance it is quite impossible to decide.

« Blood from this patient fails to give a Wasserman reaction ».

(Signed) DOUGLAS SYMMERS,
acting Pathologist to New York Hospital.

Dr. JAMES EWING's report of tumor removed at my operation January, 15, 1912, showed it to be undoubtedly a « Round-celled sarcoma ».

Pathological report, dated April 1912 :

« Sections show a diffuse growth of medium size rounded cells. Nuclei are moderately hyperchromatic; mitoses are occasionally seen. No reticular stroma is visible but the tumor is infiltrating the muscular and fat tissues after the manner of a malignant growth.

« Diagnosis : Lymphosarcoma ».

(Signed) JAMES EWING.

CASE 4. — *Inoperable round-celled sarcoma of the tonsil and neck successfully treated with the mixed toxins.*

A. L., age 11 years, Hartford, Conn. The patient was referred to me by Dr. WILLIAM R. PORTER of Hartford on November 8, 1906. The patient had always been in good health, except that she had frequent attacks of tonsillitis. A year ago she had a small swelling in one of the glands on the right side of the neck. The mother does not know whether it entirely subsided or not. Two months ago she noticed considerable enlargement in this region, which increased rather rapidly. When examined by Dr. PORTER in the latter part of October he discovered a large tumor, apparently originating in the right tonsil and nearly blocking up the pharynx. She was examined by Dr. Mc KNIGHT and a number of other physicians in Hartford, and all considered the tumor inoperable. The patient was referred to me by Dr. PORTER on November 8, 1906. Physical examination at this time showed a growth the size of half a hen's egg, on the right side of the neck, involving the pharynx wall and tonsil, nearly blocking up the passage. On the opposite side of the neck, just below the angle of the jaw, there is a tumor about the size of a small hen's egg, fairly movable, smooth in outline, fairly firm in consistence, skin not adherent. Diagnosis : Round-celled sarcoma of tonsil and neck. The toxins were begun November 9, 1906, and continued with two or three intervals to rest, one of three weeks in duration, up to the middle of May, 1907, the patient receiving in all between eighty and ninety injections, nearly all of which were given in the pectoral region; a few were given into the tumor of the neck, but none into the tonsil. After two or three weeks' treatment there was a marked softening of both neck and tonsil tumor. Examination in consultation with Dr. W. L. CULBERT; the latter removed a portion of the

tumor of the tonsil, and it was found that the central portion of the same had become entirely necrotic, and several drams of broken-down tumor tissue were curetted out. I also removed some tissues from the tumor of the neck, which also proved softened and necrotic in the center. Both specimens were examined at the Loomis Laboratory by Drs. TRACY and BUXTON, and both proved to be roundcelled sarcoma.

This patient was rather susceptible to the toxins, and was rarely able to stand more than two or three minims without a severe chill, followed by a temperature of 103° to 105°. The highest temperature was 106°.

In two months the tumor of the tonsil and the neck had entirely disappeared. Shortly afterward a new swelling developed in the neck, about one inch higher up. This swelling persisted for a long time in spite of continued and severe treatment. She also developed a small glandular tumor on the other side of the neck beneath the sternomastoid muscle. In February, while taking the treatment, she had a severe attack of herpes, involving the right pectoral region and entire right arm. This was extremely painful, and she was unable to take the treatment for about three weeks. In the early part of May there still remained some swelling in both sides of the neck, rather deeply seated, underneath the sternomastoid muscle, and I decided to explore under ether. I found the swelling consisted entirely of broken-down necrotic material which had not found an easy exit. Some of the tissues from both sides were sent to Dr. TRACY of the Loomis Laboratory, and microscopical examination showed no evidence of sarcoma remaining. The wound quickly healed. The patient was shown before the Hartford Medical Society on May 27, 1907, apparently perfectly cured, and again before the Clinical Congress of Surgeons of North-America, in November, 1912, in good health. My last examination was made December 2^d, 1913. She is now well seven and-a-half years after treatment.

CASE 3. — *Sarcoma of the mediastinal glands. Clinical and X-ray diagnosis.*

G. B., male, 53 years of age, referred to me by Dr. G. R. BUTLER of Brooklyn on November, 25, 1908, for what was believed to be a

malignant tumor of the mediastinum. There was no family or personal history of tuberculosis; no history of syphilis. He had first noticed huskiness of voice fifteen months before, which gradually increased; some dyspnoea, which slowly became more pronounced. Physical examination on November 25, 1908, showed dullness over the whole mediastinum; the abdomen was distended, some ascitic fluid being present. No swelling of feet and hands. General condition good; no loss of weight. Just above the clavicle and attached to the sterno-clavicular portion of the sterno-mastoid muscle there was a small, hard gland. No enlargement of thyroid. A careful X-ray examination made by Dr. CHAS. EASTMOND of Brooklyn, on September 29, 1908, showed a large tumor occupying the mediastinal region. The patient was immediately put upon the mixed toxins which were given under my direction.

A second X-ray examination made December 31, 1908, showed some diminution in the size of the tumor. The toxins were continued for one-and-a-half year with occasional intervals of rest. X-ray examinations made from time to time showed a slow, but continued diminution in the size of the tumor with decrease in density, as found by Dr. EASTMOND.

My last examination of the patient, made March 13, 1911, two-and-half years afterward, showed his general condition perfectly normal; the hoarseness had remained about the same; the dullness had markedly decreased. — X-ray examination showed a decrease in size and density of the tumor.

The last report I received from Mr. BAAND, February 14, 1914, nearly five-and-a-half years later, states that he is still in good health.

Cass 6. — Round-celled lympho-sarcoma of the neck and supra-clavicular glands recurrent, inoperable.

A. P., 2 years and 10 months old. Referred to me by Dr. E. J. McKNIGHT of Hartford, Conn., in March, 1902. Primary tumor removed by Dr. McKNIGHT at the Hartford Hospital on January 27, 1902. No examination of the specimen was made, but the tumor rapidly recurred and a second operation was done in March, 1902. The specimen removed at this time was examined by Dr. W. R. STEINER, pathologist at the Hartford Hospital, who made the diagnosis of small round celled sar-

coma. The disease was considered too extensive for removal. The patient was first seen by me on March 8, 1912, when I found a series of tumors extending from the clavicle to the mastoid bone on the right side; the submaxillary and axillary glands on the right side were also involved; the clinical appearance of the disease was typically sarcomatous. I advised the toxin treatment which was carried out by Dr. McKNIGHT for about three months. Immediate improvement, followed by complete disappearance. Patient well at present, over eleven years afterward.

Shown before the Congress of Clinical Surgeons of North American on November 12, 1912.

CASE 7. — *Small round-celled sarcoma of the neck. Entire disappearance under three months treatment with the mixed toxin. Patient, well as present five years later.*

P. K., male, 41 years old, heavy smoker. First noticed a lump in the submaxillary region in April, 1909. This grew rapidly, and by June had reached the size of a hen's egg.

On June 11, 1909, the patient was admitted to the Roosevelt Hospital to the service of Dr. CHARLES H. PECK, who stated that he found a very vascular tumor which had invaded the periosteum of the lower jaw. There was also marked infiltration of the muscles and skin.

Dr. PECK could not make a complete removal, and gave a hopeless prognosis. A microscopic examination was made by Dr. HODENPYL, the pathologist to the hospital, and he pronounced it a small, round-celled sarcoma, highly malignant.

The patient was referred to me by Dr. PECK a few weeks after operation, for the toxin treatment, which was carried out under my direction by Dr. LIPSET, the family physician.

Shortly after the treatment was begun, the infiltrated area in the region of the cicatrix began to soften and recede, and at the end of three months it had entirely disappeared. The patient has remained well up to the present time, four-and-a-half years after the tumor disappeared. There is no trace whatever of the disease at present (January 1914) and he is in good general health. The toxin was kept up in small doses, with intervals of rest, for one year.

Patient was shown before the Clinical Congress of Surgeons of North America in November, 1912.

CASE 8. — *Lympho-sarcoma of axilla.*

Mrs. J. G., 45 years. Family history good. In December, 1905, first noticed a lump in the left arm, which slowly increased in size until given in March, 1906, when it was removed by operation. Microscopical examination made by the pathologist of West Pennsylvania Hospital, whose report reads :

The tumor is composed of small round cells of about the size and appearance of mononuclear leucocytes (sarcoma cells) with a moderate amount of intercellular substance and shows the reticulum and stroma formed by branching stellate forms, which is characteristic of lympho-sarcoma.

The patient was referred to me March 25, 1906, by Dr. K. I. SANES of Pittsburg, Pa., who stated that the glandular tumor was adherent to the axillary vein; but it was impossible to state from examination whether or not the axillary vein itself was involved. I advised the use of the mixed toxins, which were started immediately and continued for a number of weeks by the family physician. Two years later (March 23, 1908) I received a letter from the patient's husband, which stated : « Mr. G. is quite well, Has been troubled recently with some rheumatism and during summer had severe attack of bronchitis followed by intercostal neuralgia brought on by the coughing. On convalescing partly, she went to Cape May for six weeks, and a specialist there, who treated her with electricity, stated that her condition had nothing to do with her old trouble. »

The operation was regarded as incomplete.

In a letter received from the patient's husband, dated January 20, 1914, he states « Mr. G. has never had a return of the trouble for which the toxin treatment was administered ».

CASE 9. — *Round celled sarcoma of the axillary glands (endothelioma),*
toxins used after incomplete operation.

P. B., male, 67 years old, family history negative. Patient was referred to me in January, 1911. Three years ago he first noticed an enlarged gland in the axilla. This slowly increased in size until a month ago when following an attack of grippe, it increased in size.

January 31, 1911, physical examination showed a tumor 2 1/2 by

3 inches in diameter, made up of a number of enlarged glands, varying in size from that of a hazelnut to a walnut. The glands were more or less discrete, and resembled those found in Hodgkins Disease. The skin was normal in appearance and not adherent. On February 1, 1911, I removed the glands as thoroughly as possible up to the clavicle. The operation was a difficult one and it was certain that several of the diseased glands had been left behind.

Pathological Report made by Dr. EWING, reads : « The tumor is a sarcoma in lymph nodes ». — The report of Dr. WM. CLARK (pathologist of the General Memorial Hospital) states : « Round-celled Sarcoma ».

Immediately after the operation, the patient was put upon the mixed toxins of erysipelas and bacillus prodigiosus, which were given for three weeks at the hospital, and later continued by the family physician for six months.

After a more careful study of the tumor issue, made by Dr. EWING in 1913, he concluded that the tumor was an endothelioma. November 11, 1912, nearly two years later, the patient's physician state that he was perfectly well.

Later note : According to a letter received from Dr. JOHN C. FERBERT, of Los Angeles, on October 18, 1913, Mr. B. came to him in the early part of September, with a tumor below the clavicle and some swelling in his arm. Dr. FERBERT believed it to be a recurrence, and removed a gland about the size of a robbin's egg from underneath the pectoralis minor muscle; it was firmly attached to the subclavian vein. No other glands could be palpated. The toxin treatment has been resumed, as a prophylactic.

A further specimen of the case was sent to Dr. EWING who reported, on January 29, 1914 :

The tumor of supraclavicular glands in the case of Dr. F. proves to be a true lymphosarcoma. It is composed of rather large round cells quite different from the spurious lymphosarcomas which resemble Hodgkin's disease.

A letter from Dr. FERBERT, dated January 28, 1914, states :

Mr. B. is feeling very well and his condition is satisfactory, except that the arm remains swollen, owing, I believe, to the fact that in removing the last gland, the axillary vein was torn, necessitating suturing the vein.

CASE 10. — *Inoperable recurrent sarcoma of the parotid, face and neck.*

F. W., male, 27 years. Family history of cancer on mother's side; personal history negative, except that he had a severe attack of typhoid fever in 1895, after which he developed what his family physician, Dr. M. STAMM, called « noma » or gangrenous inflammation of the right cheek. He states that the lips grew together so completely that that had to be cut apart, at which time a cartilaginous tumor about the size of a small hickory nut was found and removed. The lips immediately grew together again and a year later, a tumor, the size of walnut was removed from the right cheek just below and anterior to the ear. The tumor promptly recurred and was removed four times in six years. Two years later, another recurrence having taken place, he submitted to a paste treatment of some sort in Cleveland. The tumors came away, but the one of the face recurred six months after the paste treatment and grew very rapidly. Early in 1909, he went to consult the MAYO'S, who advised against further operation and referred him to me for the toxin treatment. The same advice was also given him by Dr. NANCREDE, of Ann Arbor, who refused to operate. At this time, in addition to the large tumor of the parotid, occupying the entire right side of the face, there was another tumor, the size of a hen's egg beneath the jaw, causing considerable difficulty in breathing. The patient came to me in February, 1909, and was admitted to the General Memorial Hospital. Physical examination at this time showed a large tumor, occupying the whole side of the face, most prominent in the parotid region, extending down beneath the chin. There was a large amount of scar tissue evidently resulting from the paste treatment. The skin itself was not adherent to the tumor, which was firm in consistence, certain areas having an almost cartilaginous « feel », in others being softer. It was entirely inoperable. The toxin treatment was started on February 23, 1909 and continued for three months, during which time he received in all fifty-eight injections, in doses ranging from $1\frac{1}{2}$ to 7 minims. Both the filtered and unfiltered toxins were used; thirty-seven injections were made into the pectoral region, twenty into the tumor itself, one into the thigh with very good reactions, the temperature going up as high as 104°. In May I advised him to return home and have the treat-

ment continued by his family physician, Dr. DEEMER. He states that he had some very severe reactions during the summer a temperature of 105 or 106°, following the injection of $\frac{1}{2}$ minim given into the tumor direct, the most severe reaction he ever had. In October he returned to me for a three weeks' course of toxin treatment. Examination at this time showed very marked diminution in size; the difficulty in swallowing and breathing had entirely disappeared and his general condition was good. The patient then returned home, no further treatment was given.

In a letter, dated January 16, 1914, five and one half years after the treatment was discontinued, the patient states that while the tumor has not disappeared, it remains exactly the same size as in the fall of 1909. «Dr. DEEMER and I take measurements each year by means of callipers and the measurements have not varied $\frac{1}{16}$ inch in all this time.»

I have been unable to get a section from any of the tumors removed at the previous operations, but the history of five removals, each followed by a quick recurrence is, I believe, sufficient evidence that the tumor was of malignant nature, probably a mixed-celled sarcoma of the parotid.

CASE 11. — *Round celled sarcoma, glands neck.*

H. W. Patient had been in good health until the early part of May, 1913, when he noticed a small painless lump appear just under the jaw on the right side, in the region of the submaxillary glands. The nodule grew rapidly in size and was operated upon by Dr FRED'K B. SWEET, of Springfield, Mass., who found a tumor about the size of a pecan nut, which shelled out of its capsule like a pea from its pod. There was no infiltration of the surrounding tissues nor was the tumor attached to the bone. Microscopical examination proved the growth to be round-celled sarcoma. Shortly after the operation, another gland developed beneath the right sterno-mastoid muscle. This was removed by operation, and found lying between the carotid and internal jugular vein, about the size of a small cherry. A portion was removed and sent to Dr EWING, whose report reads;

June 12, 1913.

The material shows a process which I should call lymphosarcoma. It is somewhat peculiar in that the cell type is not very typical, but

mitotic figures are abundant and the structure of glands is obliterated. I assume that there is no leukamia.

Within a week of this operation a rather diffused swelling developed at the site of the incision. No attempt at removal was made for fear of injuring the facial nerve. Patient entered the General Memorial Hospital, June 5, 1913, for the mixed toxin treatment. The toxins were given in gradually increasing doses but no reactions were obtained until 8 minims had been reached. There was no temperature although he became very much depressed and felt bad after 5 minims dose. During this period, two to three very small glands appeared at the site of the second operation over the carotid vessels, and gradually grew until they had reached the size of a hazelnut. After the first reaction was obtained there seemed to be no further increase in size of growths. Patient returned home July 26th, where the toxins were continued by his family physician Dr SHORES, three times a week in doses ranging from 7 to 9 minims. Reaction occurred about every, third day. On my return from Europe, end of August, patient came to me for examination and advice. I found that the glands in the neck had not increased any in size during my absence and there was no return of the tumor in the submaxillary region, which had disappeared under the toxins. In order to lessen the severity of the treatment, and also in the hope of increasing the chances of controlling the disease, I decided to again operate and remove the tumors in the carotid region, for which purpose, patient re-entered the hospital on September 4, 1913. I found them very deeply placed about the carotid vessels, and removed three growths ranging from the size of a pecan to that of a hazel nut. Examination showed tumors to be round celled sarcoma. There were undoubtedly a few smaller growths situated higher up, which were not removed; the wound was fulgurated five minutes. The toxins were immediately resumed and the dose pushed to 9 minims which gave a good reaction. On September 11th, the patient left the hospital and returned home where the treatment was given three times a week for two months, after which he received one week's respite. He came to see me on December 2, 1913, at which time I found his weight to have increased considerably, and the condition of his neck revealed no trace of the tumor.

Last examination made March 13, 1914, shows no trace of recurrence general health excellent, weight 206 pounds. He has been taking the toxins regularly since May, 1913, now in doses seven minims twice a week along which does not interfere with his business.

CASE 12. — *Hound-celled sarcoma of the neck.*

Dr P. V. In the early part of 1913, patient noticed a swelling in the neck, starting midway between the chin and thyroid; considered at first an inflammatory process by one, phlegmon by another physician. Operation by Dr RUSSELL S. FOWLER of Brooklyn, and after microscopical examination the disease was pronounced infective granuloma. Later it was pronounced round-celled sarcoma. Four weeks after the operation, a recurrence set in which grew rapidly, soon reaching the size of a fist, and extending from the mastoid to the clavicle.

The case was considered inoperable by Dr FOWLER, who then started the toxin treatment, April 10, 1913. After five to six injections the tumor began to soften, and it opened spontaneously, discharging, necrotic material and gradually decreasing in size so that in the early part of May, Dr. FOWLER regarded the trouble as practically cured, and he diminished the size of the dose of toxins. When he had gone back from 14 $\frac{1}{2}$ minims to 8 $\frac{1}{2}$ minims, the tumor began to increase again very rapidly, whereupon the doses were again increased. I first saw the patient on the 15th of May, and on physical examination found an old cicatrix 2 inches long, about an inch below the angle of the jaw, extending over to the chin. There were two recent cicatrices at the site of the old healed sinuses. In the anterior portion of the neck, beginning a little to the left of the median line and extending downward to the angle of the jaw, was a mass about 2 $\frac{1}{2}$ inches in diameter laterally, very firm in consistence and much harder than ordinary sarcoma, more like carcinoma. There were several other smaller and discrete tumors in the cervical and supra-clavicular regions. Skin adherent only in the region of the cicatrix, and not reddened. Tumor not attached to the trachea or thyroid cartilage. General condition good, but the patient had lost 15 pounds in weight. I urged pushing the toxins to the limits of safety, and after increased doses his condition quickly showed signs of improvement. The improvement, continued, and at the time of my last examination, July 17, 1913,

the tumors in the cervical and submental regions had almost completely disappeared, and his general condition was good. The dose of the toxins had been carried up to 20 minims given in the pectoral region.

Physical examination January 20, 1914, shows the neck entirely normal. There is no suspicion of any enlarged glands. The patient's weight has increased from 212 to 222 lbs.

CASE 13. — *Round celled sarcoma of tonsil with metastases in neck. Entire disappearance under toxin treatment, no recurrence three and-a-half years later.*

C. W., 56 years of age. Family history. Uncle died of cancer of leg. Patient's general health always good. Referred to me by Dr. Skeels, of St. Albans, Vermont, on May 26, 1910. He had smoked a great deal, but stopped smoking six weeks ago. He first noticed a swelling in the right tonsil two months ago; two weeks ago noticed an enlargement of the gland in the right side of the neck; treated by throat specialists during which time the tumor increased steadily and rapidly, had been pronounced an inoperable malignant tumor by four prominent surgeons of Montreal. Physical examination by me on May 26, 1910, shows the right tonsil enlarged to the size of an almond, ulcerated on its posterior surface. The tumor was very hard on palpation, resembling carcinoma rather than sarcoma; there was a hard, movable gland the size of an English walnut in the right cervical region, anteriorly to the sterno-mastoid muscle. The patient was admitted to the General Memorial Hospital and remained in the hospital for about six weeks. A portion of the tonsil was removed for microscopical examination and proved to be round-celled sarcoma by Dr. W. C. CLARK, Pathologist to the Hospital. The injections were practically all made into the pectoral region and the doses ranged from $1\frac{1}{2}$ minim to 5 minims, with fairly severe reactions from the larger doses. The tumor in the neck first became softer and more movable; at the end of a week it began to decrease in size with final disappearance under four weeks of further treatment. The tumor of the tonsil diminished more slowly but at the end of two to three months this, too, entirely disappeared. A letter from the patient's physician, dated March 19, 1911, stated: « He is at present perfectly

well; there is absolutely no sign of any growth in his tonsil; his recovery here is considered as almost miraculous ».

Later note : A letter received from the attending physician Dr. E. J. MELVILLE, under date of July 10, 1913, states :

There is no return of the tumor in Mr. W's case and no particular change in his condition from what I reported to you six months ago. The tumor, has not returned. In fact the tonsil and peritonsillar tissue is normal. His only ailment is a progressive dementia, probably caused by ischaemia of the brain.

I am enthusiastic about the serum and you may count this case as a complete cure, with no return to date.

Under date of January 14, 1914, Dr. MELVILLE writes :

There has been no return of the sarcoma of the tonsil, which disappeared under the toxin treatment four years ago.

Mr. W. is about the same as when I wrote you last, suffering from ischaemia of certain areas of the brain, which causes a form of brain softening, and progressive dementia, of a mild idiotic type. This condition is probably due to arterio-sclerosis, from which disease he has suffered for ten years.

His appetite and general physical condition have not materially changed in the past two years.

CASE 14. — *Small round-celled sarcoma of the tonsil with extensive metastases on both sides of neck. Entire disappearance under toxin treatment. Recurrence one year later.*

Mr. C., 42 years of age. Marked loss of weight; referred to me by Dr. SELANDY, Boston, May 29, 1906. Physical examination at this time showed a large tumor in the right tonsil nearly blocking up the pharynx; it had the typical clinical appearance of sarcoma; metastases occupied both cervical regions extending down nearly to the clavicle; general condition markedly deteriorated. The prognosis seemed so hopeless, that no microscopical examination was made. The toxins were given in to the pectoral region and pushed to extremely high doses, as much as 20 minims of the unfiltered preparation being given which were followed by severe reactions, the temperature rising to 104 to 105°. There was considerable decrease in the size of the tumors while he was in the hospital, but his general condition

was bad and he continued to lose weight under the treatment, that it was not considered wise to continue and after he had thirty-one injections he was sent home for an interval of rest. The improvement continued steadily after he left the hospital and at the end of four months the tumors of the tonsil and neck had entirely disappeared. The patient stated that he had taken some patent medicine for a time after he left the hospital. In June, 1907, a little over a year later, there was a recurrence in the right side of the neck, and he again returned to me. At this time there was a smooth globular swelling in the sub submaxillary region about the size of a small hen's egg, moderately soft in consistence and not very firmly attached. It had the typical clinical appearance of a sarcoma. I removed the tumor, and microscopical examination by Drs. B. H. Buxton and E. K. Dunham showed it to be a small round-celled sarcoma. The patient's general health was perfect. I advised resumption of the toxin treatment, but the patient refused and returned home. Other tumors quickly developed in the neck and grew with great rapidity, causing death within a year.

This case, I believe, is of *extrême importance*, inasmuch as it shows that a tumor of high malignancy, the diagnosis of which was confirmed by the fatal issue, entirely disappeared together with the metastases under three months' treatment with the toxins. The subsequent recurrence with the diagnosis this time confirmed by microscopical examination removes all doubt of the nature of the primary tumor.

CASE 15. — *Round-celled sarcoma of the neck.*

F. W., male, 58 years of age, referred to me by Dr. G. H. Gray of Lynn, Massachusetts, December 21, 1908. Family history negative. Personal history. Two years before patient noticed a small painless tumor in the right cervical region. This grew slowly at first, but more rapidly later, and at the time of the first operation, November 24, 1908, by Dr. Gray, the tumor had reached the size of a small egg. It was found impossible to make a complete removal. At the time the patient came to me (December 21, 1908), there was a well-marked recurrence, and the condition was inoperable. The patient was admitted to the general Memorial Hospital on the 25th of December, 1908, and received eleven treatments under my care. He

was then advised to return to his home, and the treatments were continued by Dr. GRAY. He had eighty-two injections altogether, the highest dose being $4\frac{1}{2}$ and $4\frac{1}{2}$ minims; the temperature ranging between 99.5° and 100° . At the end of six months the toxins were given but once a week. The treatment was continued for nearly a year altogether. Examination, November 11, 1909, nearly a year



Fig. 2 (Case 15).

after the treatment was begun, showed a 3 inch cicatrix over the interior sterno-mastoid region, soft, pliable, with no evidence of a tumor remaining. General health was perfect. In a letter received from Dr. GRAY (dated April, 9, 1911) he states that the patient is well at present and in perfect general health, nearly two and one-half years later. October 9, 1913, Dr. GRAY writes : « M. W. is alive and well ».

CASE 16. — *Lymphosarcoma of neck, round-celled.*

Mr. L. referred to me by Dr. STANLEY STILLMAN of San Francisco in April, 1908. The diagnosis was confirmed by microscopical

examination made by Dr. OPHULS of San Francisco and Dr. WELCH of JOHNS HOPKINS University.

A number of glands of the neck were involved. An incomplete operation was performed and the remainder of the disease disappeared under the toxin treatment which was kept up for six months. Two months after disappearance of the tumors, the disease returned locally, but soon invaded the axillary glands, and later abdominal metastases caused death within a year.

CASE 17. — *Sarcoma of the lymphatic glands-inguinal.*

E. C. B., 21 years of age, male always well until January 1908, when he was struck in the left groin by a lever. One week later he noticed a swelling at the point of injury. This increased steadily in size until February 2, three weeks after the injury, a tumor was removed by Dr. DUDLEY CARLTON of Springfield, Mass. The microscopical examination was made by Dr. J. F. BUTLER of Springfield, Mass. who pronounced it small, roundcelled sarcoma. A recurrence took place shortly afterward in the inguinal and iliac glands and the patient was referred to me for the toxin treatment. Physical examination March 26, 1908, showed is general condition good. Examination of the left groin revealed enlargement of the inguinal and superficial iliac glands; skin was not adherent and there was no tenderness; the tumor was of moderately firm consistence. The patient entered my service at the General Memorial hospital, where the toxin treatment was at once begun. The injections were in all (twenty-seven in all) were made in the buttocks and continued for two weeks in doses ranging from $1\frac{1}{2}$ to 5 minims followed by well marked reactions a temperature up to 104° . At the end of this time the tumors had almost completely disappeared and he was allowed to go home with the advice to have the toxins continued by his family physician. The treatment was carried out rather irregularly during the summer and in October of the same year, he returned to my service with evidence of a recurrence. The toxins were again administered for a period of three and a half weeks, partly into the tumor, and partly into the buttocks, with good reactions. He received nineteen injections during this time. He was then sent home and urged to have the treatment continued for another three to four months. When-

last heard from (January, 1914), six years after operation, he was in good health and free from recurrence.

CASE 18. — *Intra-abdominal lympho-sarcoma, involving mesentery, mesenteric glands and portion of small intestine.*

Mrs. W., 25 years of age, was operated upon in November, 1913 by Dr. Wm. M. CONANT, of the Massachusetts General Hospital, for an abdominal tumor. Exploratory operation showed a tumor, the size of a closed fist, occupying the posterior parietal part of the mesentery and a portion of the small intestine. It was so extensive that no attempt was made to remove it. A portion was excised for microscopical examination, which was made by Dr. W. F. WHITNEY and Dr. A. C. POTTER, the former the pathologist of the Massachusetts General Hospital, the latter of the Harvard Medical School, — who pronounced it round — celled sarcoma. In December, 1903, the patient was referred to me, by Dr. CONANT and I immediately put her upon the mixed toxins, giving fixe to six injections a week, also adding a number of X-ray treatments. The tumor immediately began to decrease in size and at the end of four months it had entirely disappeared. At this time the patient developed a high temperature and acute abdominal symptoms, pointing to a local peritonitis, due — as it proved — to a necrosed portion of the small intestine involved in the tumor. She was desperately ill and hope of life was abandoned for more than a week. Thereupon a faecal fistula developed and she slowly recovered her health. She ran irregular temperatures until the latter part of July, when the temperature fell to normal. The toxins were given for a considerable time after recovery, by her family physician, Dr. WILLIAM WILSON of Pawtucket, R. I. In a letter received from Dr. WILSON, dated February. 13, 1906, he stated that evidence of a return had appeared in the spring of 1905, as shown by accumulation of fluid in the peritoneal cavity. Dr. CONANT was called in and established permanent drainage; at which time he discovered several retroperitoneal growths. The condition gradually became worse and the patient died a few months later.

CASE 19 — *Sarcoma of the groin (clinical diagnosis only).*

H. P., 7 years old, was referred to me by Dr. E. P. SWASEY of New Britain, Conn. Family history negative. Previous health good

Patient received a kick in the right groin by another boy in August, 1910. Four days later a small lump appeared in the groin, and gradually increased in size. One month later it had reached the size of an egg, and was removed by Dr. SWASEY, who made two incisions in the right groin. No microscopical examination was made. The wound never healed properly; there remained a sluggish ulceration at the site of the cicatrix, with gradual thickening of the surrounding tissues; pelvic glands involved. The patient's general condition was good, and there was no lameness.

Physical examination on November 8, 1910, showed considerable swelling of the whole upper part of the thigh and inguinal region. Just above Poupart's ligament there were two incisions one about 2 inches long, and the other, 2 1/2 inches, showing no tendency to heal, but filled with sluggish grayish granulations. Palpation above Poupart's ligament showed a hard gland the size of an English walnut. Clinical diagnosis sarcoma.

The toxins were advised, and given for four weeks, at the end of which time the tumors had markedly decreased in size, becoming more freely movable, and semi-fluctuating and later were curetted, under ether anaesthesia at the Hospital for Ruptured and Crippled. The tissues were too broken-down to make any positive histological diagnosis. During 1911-1912, the patient had two decided attacks of erysipelas in the right leg. In a letter received from Dr. SWASEY, dated January 17, 1914, (three and one quarter years later), he states : « I have seen the patient, H. P. today, and have the pleasure of reporting that he is in excellent health. »

CASE 20. — Hodgkin's disease. Involvement of cervical axillary and inguinal glands. Enlargement of spleen and liver. Entire disappearance of palpable lesions under mixed toxins alone. Recurrence six months later, ending fatally.

G. K., male, 24 years of age. First noticed enlargement on right side of neck in the fall of 1906. Patient entered the General Memorial Hospital, October 10, 1907. Examination at this time showed a tumor occupying the whole right cervical region from the mastoid to the clavicle and from the median line in front to nearly the median line behind; a similar enlargement of the glands of the axillæ and

groins. The spleen was greatly enlarged, extending up to about two inches below the costal arch; liver slightly enlarged. The patient was put upon the mixed toxins of erysipelas and bacillus prodigiosus; only systemic injections into the pectoral regions were given, the initial dose being $1\frac{1}{5}$ minim, which was gradually increased to one and one-half minim, which latter dose produced a temperature of 105.6 degrees. On November 15th, slightly over one month from the time of his admission to the hospital, all tumors had practically disappeared; only a few minute nodules could be felt in the right side of the neck, and these had entirely disappeared by November 20th. He received nineteen injections in all. He refused further treatment. A little over six months later the disease recurred and proved fatal within another six months.

In this case the diagnosis was clinically confirmed by Dr. W. K. DRAPER and microscopical examination was made by Drs. W. C. CLARK, pathologist of the hospital, and JAMES EWING, Professor of Pathology at Cornell University Medical School. Both pronounced it unquestionably Hodgkin's disease.

Cases of sarcoma originating in Bern (Osteosarcoma).

In thirty-one of my personal cases, the disease was primary in the bones, chiefly the long bones.

It is important to note that in this group of cases only six were of the so-called giant-celled, or less malignant type. One of these cases, a periosteal sarcoma of the humerus, was of the extremely malignant type characterised by Bloodgood as « bone aneurism ». Spontaneous fracture of the humerus had occurred and the patient had been regarded by Dr. FINNEY of Baltimor, as beyond shoulder-joint amputation. After the tumor had apparently disappeared under the toxin treatment, a recurrence took six months later place near the shoulder and amputation finally had to be performed. In spite of a subsequent and very extensive recurrence in the pectoral region, which was removed by operation, followed by the toxin treatment for two years, the patient has remained well up to the present time, five years later.

In a considerable number of cases, nearly twenty including the cases of other men; the limb has been saved by the use of the toxins before resorting to amputation. In several of these cases the tumor was of the periosteal type, which is rarely cured by high amputation.

CASE 21. — *Very large osteo-chondrosarcoma of ilium; disappearance of tumor; recurrence seven months later followed by death.*

M., male, 23 years of age. Patient had a tumor of one year's duration, occupying a large portion of the right ilium, extending from the middle of the sacrum behind to the border of the right rectus in front, and filling up the larger portion of the right iliac fossa. He was much emaciated and rapidly losing ground. I saw the patient at the request of Drs. GEORGE F. SHRADY and F. KAMMERER, under whose charge he was, at St. Francis's Hospital. The toxins were begun in March, 1894, and continued under my direction for five weeks. Marked reactions followed the injections of the mixed filtered toxins. The tumor after a few days began to soften and break down, and a large area of fluctuation appeared. Free incision permitted the escape of much broken-down tissue and large masses continued to slough out for a considerable time. High temperature continued for a month after the injections were stopped, due to the absorption of dead tissue. At the end of this time improvement began, and he rapidly regained his health and strength. By November 15, 1894, the tumor had apparently entirely disappeared and the patient had gained, fully forty pounds since June, and had resumed his work. He was shown before the Surgical Section of the New York Academy of Medicine, and Dr. SHRADY regarded him as cured. In December, 1894, there was evidence of a local recurrence, and in spite of further treatment with the toxins the tumor steadily increased in size. His condition was regarded as hopeless, though he was able to walk about with a cane.

No microscopical examination of the original tumor was made, but the rapid growth and enormous size made the diagnosis clear, while the recurrence and prospective fatal issue confirm it. The patient died in July, 1896.

CASE 22. — *Recurrent inoperable spindle-celled sarcoma of iliac fossa, probably starting in the ilium. Entire disappear under the mixed toxins patient in good health twelve years later.*

Mrs. D, 40 years old. Family history negative.

In the early part of 1895 patient began to have sharp stinging pains in the right iliac region. In May, 1895, she discovered a tumor in this

region, which steadily increased in size, and on October 19, 1895, Dr. JOHNSTON, of Boston, performed an exploratory laparotomy. He states, « A tumor was found in the right iliac fossa about the size of a cocoanut, attached to the ilium, as well as to the abdominal wall, and totally inoperable. Its exact point of origin could not be made out, but from the exploration and subsequent examination, I am convinced that it started from the inner portion of the crest of the ilium ». A part of the tumor was excised and examined by Dr. WILLIAM F. WAITNEY, pathologist to the Massachusetts General Hospital, who pronounced it « spindle-celled sarcoma ». In November, 1895, the patient was treated with injections of the mixed unfiltered toxins by Dr. FARRAR Cons, of Boston. In a letter Dr. COBB states : « At the end of six weeks' treatment the growth has entirely disappeared. »

On May 17, 1896, the patient came to me with a recurrence and entered the New York Cancer Hospital. Examination at the date showed a hard mass on the right side, extending from the crest of the ilium nearly to the level of the umbilicus and as far to the left as the median line. The tumor was apparently located in the ilium and abdominal wall. Her general health was excellent. The toxins were at once begun and continued, with intervals of rest, for three months. The outline of the tumor gradually receded toward the crest of the ilium, and when she was discharged from the hospital the tumor was not more than one-fifth its original size. She left with the understanding that she was to return in the fall to haul the injections resumed. She was readmitted to the hospital in November. Examination showed the tumor to have increased considerably in size during the interval of rest, but on beginning the treatment the tumor at once began to shrink. Whenever the injections were made the patient noticed a peculiar burning feeling in the tumor, and this was true whether the injections were made into the abdominal wall or into the thigh. The abdominal wall was so thick with fat that few of the injections were made into the tumor itself. This patient was one of the very few I have seen in who the toxins always produced very severe irritation in the skin. After each puncture a hard, indurated and very painful area the size of a half dollar would appear, and this would not pass away entirely for several days. When she left the hospital, June 1897, the tumor had remarkably decreased in size, and disappeared entirely a few months later. I examined her twelve

years after the treatment, at which time she was in good health, with no trace of a tumor.

CASE 23. — *Round-celled giant-celled sarcoma of the radius; toxins given for six weeks; patient well at present nearly two and one-half years later.*

F. S., female, 25 years of age; married; no tuberculous history; no history of cancer in family; no trauma. Six or seven months ago the patient noticed pain in the right thumb; shortly afterward she observed a swelling in the lower end of the radius. She first consulted a physician five months ago and was treated for a time for sprain and the arm was put in a plaster cast. Two weeks ago she consulted Dr. IRVING HAYNES of this city, who regarded the condition at first as one of tubercular disease. On February 13, 1911, an exploratory operation was performed and a portion of the tumor removed, which proved to be a round-celled sarcoma. Before amputating the arm, Dr. HAYNES believed it wise to give the patient the benefit of a trial with the mixed toxins and referred her to me on February 20, 1911. Physical examination at this time showed marked enlargement of the lower end of the radius for a distance of about 3 inches; on the inner aspect of the forearm, about one inch above the lower end of the radius was a recent incision from which there projected a fungating mass, with considerable sero-sanguinolent discharge. She complained of a great deal of pain. On February 23rd, she was admitted to the General Memorial Hospital and the toxins were begun. The initial dose was $\frac{1}{2}$ minim, which was gradually increased up to the point of producing a marked chill. At the end of one week of systemic injections, the latter were given into the tumor direct every other time. The highest dose into the tumor has been 3 minims; the highest systemic dose 5 minims. At the end of one week of treatment the condition showed marked improvement, which continued steadily. Examination on March 25, shows the radius to have returned to normal size; the fungating mass has entirely disappeared and the wound healed in three weeks. She is perfectly well January, 1914, doing her own work. Duration of treatment six weeks.

Patient was shown before the Clinical Congress of Surgeons of North America, November, 1912.

She is now well more than two years after treatment.

CASE 24. — *Sarcome of radius. Round-celled (giant celled), amputation advised but refused by patient, entire disappearance under six weeks toxin treatment, patient well five and three quarter years later.*

M. F., female, 26 years of age. Family history negative. Several years ago fell and injured left wrist. In the spring of 1908 tripped and fell, injuring the same wrist. Examination by her family physician showed a fracture of the wrist. Two weeks later she went to the New York Hospital and X-ray examination showed disease of the bone probably sarcoma. On May 1, 1908, an operation was performed by Drs. POOL and STEWART; the tumor being curetted out on either side. Microscopical examination made at the Pathological Department of the New York Hospital, May 1, 1908, proved the growth to be a giant-celled sarcoma. On May 18, there was no evidence of union and amputation was advised, but refused. The patient then came under my care for the treatment with the mixed toxins. After six weeks of treatment perfect union had occurred and the patient is in good health at the present time, four and a half years later. My last examination was made December 2, 1913.

CASE 25. — *Recurrent inoperable sarcoma of ilium, giant-celled. Complete recovery under toxin treatment.*

Mrs. X., 30 years of age. F. H. negative. In February 1908, the patient had a severe fall upon the ice striking upon the left buttock and ilium; severe and continued local pain followed the accident. In April, two months after the injury, a hard swelling appeared in the ilium at the site of the injury. This steadily increased in size and by September it noticeably interfered with walking. A few weeks later, she was operated upon by Dr. ANDREW J. McCOSH at the Presbyterian Hospital of New York, who found a tumor originating in the upper and outer portion of the ilium, but too extensive for radical operation. Microscopic examination by this Pathologist of Presbyterian Hospital showed it to be sarcomagiant-celled. X-ray treatment was advised and

begun shortly after the operation and continued until June 1909; slight X-ray toxæmia occurred. In June 1909 radium was used by Dr. ABBE of New York on several occasions and in December by Dr. WICKHAM of Paris. In January 1910 she was again treated by Dr. ROBERT ABBE and in July she went abroad and received a further radium treatment by Dr. WICKHAM. At this time a very large amount of radium, the largest that could be obtained, was used for ten hours at one time.

A sinus had persisted since the first operation in the fall of 1908, occasionally becoming blocked, causing septic temperature. The tendency to toxæmia appeared to be greatly aggravated after the application of the large amount of radium. Her general condition gradually grew worse; the pain which had been constant from the beginning, became very severe and oftentimes excruciating. The tumor of the ilium slowly increased in size and on May 1, 1911, she was referred to me by Dr. FRANK HARTLEY of New York, for the toxin treatment. Physical examination at this time showed the patient markedly anaemic and considerably emaciated, confined to the bed all the time, suffering from great pain which required large doses of morphine to control.

Physical examination showed a large swelling in the whole outer aspect of the ilium above the trochanter and extending to the anterior superior spine. There were three sinuses not far from the sacro-iliac synchondrosis. The uppermost sinus was about 6 inches long and was kept open by a rubber catheter one fourth of an inch in diameter, from which purulent discharge escaped. The remaining two sinuses, 1 to 2 inches below the first, were 3 to 4 inches deep and packed with gauze. The leg was flexed to an angle of 160° and could not be fully extended. The mixed filtered toxins were begun on May 2, 1911, the initial dose being $\frac{1}{2}$ minim, this was gradually increased until on May 22 she received 3 minims of the filtered preparation. She proved extremely susceptible to the toxins. At the time the treatment was begun, she had been running a temperature of 101° .

This dropped to normal within one day and remained so for several weeks except during the reaction following the toxins. Very soon improvement was noted in both the local and general condition; this continued without interruption.

Note (August 2, 1911): The improvement during the last month

has been very striking. Only one sinus is now discharging and that in very small quantity. The tumor of the ilium is decreasing in size and the patient's general condition is markedly improved. The temperature has been practically normal the last few weeks. She has been riding out in a motor the last few weeks; yesterday rode 30 miles; there has been a gain in weight of 2 1/2 lbs. within the last two weeks.

The tumor became more and more fluctuating, breaking down more rapidly than it was possible for the necrotic material to escape through the sinuses and in the early part of September there were beginning signs of absorption. Thereupon I made a large incision and curetted out about a pint of broken-down material. Only very little of it was sufficiently organized to permit of microscopical examination. Dr. EWING's report on this reads :

« The tumor in the X. case, diagnosed as giant cell sarcoma, proves in my sections of the material recently received, to be, as supposed, a giant-cell sarcoma. It is composed chiefly of small spindle cells in which lie many giant-cells of the epulis type. There are numerous areas of hemorrhage, and the giant-cells are most numerous in these areas. The structure is that of a tumor of moderate malignancy. Its position may render it more serious than if were in a superficial position, but histologically it is not to be classed with the more malignant or periosteal growths. »

The hemorrhage at operation was very severe and a large cavity the size of two fists, was packed with gauze. The patient made a very rapid recovery and her general condition improved markedly. She gained 20 lbs. in weight. The toxins were discontinued in the early part of September, but resumed in the latter part of December, 1911, as it was not thought the tumor had been entirely absorbed. End of January, 1912, the sinuses became blocked up and symptoms of absorption set in which required another operation. Under ether the sinuses were enlarged and considerable necrotic material evacuated with some trabeculae and free drainage established. Dr. EWING's report on this reads :

February 7, 1912.

The material is entirely necrotic, and on section shows nothing except a few isolated trabeculae.

A more severe attack of toxæmia occurred in April, 1912, requiring another operation to establish drainage. Evidently not only the

external, but also the internal portion of the ilium was involved and a large part of the sacrum, making it very difficult to get good drainage. The general condition of the patient was very greatly affected by the attacks of toxæmia, and the pain was so severe that it required very large doses of morphine to control it. Her condition became so desperate that no hope of recovery was entertained. Finally, in June 1912, she began to show slight improvement. In August the improvement became very rapid; the sinuses gradually healed, the pain disappeared and she began to increase in weight. The improvement has continued steadily up to the present time. She has gained about 30 lbs. in weight and, in November, 1912, no tumor could be found on most careful examination. She remains at present in good health, without any return of the disease. My last examination was made January 10, 1914. She was in excellent health. No trace of tumor could be found in the ilium, and the enlarged glands disappeared, she had regained her erect posture and more than former weight. This is one of the most remarkable recoveries that I have observed not so much from the very large size of the tumor, but from the fact that the patient's general condition was so extremely bad.

CASE 26. — *Osteosarcoma of sternum (clinical diagnosis).*

Entire recoveries (negative Wasserman).

M. C., male, 46 years. Referred to me by Dr. ISIDOR FELDMAN of this city. Family history good. Personal history: no tuberculosis or syphilis.

In January, 1912, he first noticed a swelling at the right side of the sternum, at about the junction of the second and third ribs, which slowly increased in size. There was no glandular enlargement and no pain. In May, 1912, he went to Mt. Sinai Hospital, where the tumor was regarded as an inoperable sarcoma, and was treated with X-rays, without improvement. A Wasserman test made by Dr. Coca, of Cornell University Laboratory, proved negative.

Physical examination, July 27, 1912, showed a tumor occupying the anterior portion of the sternum at the junction of the second, and third ribs, about the size of a goose egg; immovable, and apparently originating in the sternum itself. The skin was normal in appearance

except that there was slight dilatation of veins; the tumor was firm in consistence, and there was no sign fluctuation. The patient was referred to the General Memorial Hospital for treatment with the mixed toxins of erysipelas and bacillus prodigiosus; four to five injections a week were given in the pectoral region. At the end of two weeks' treatment, the tumor became much softer in consistence and smaller. The softening continued until September 5th, when there was marked fluctuation present and I advised an exploratory operation, and curetting, to be carried out by Dr. DOWNES my associate. Microscopical examination of the broken-down tissue removed, proved negative. Wound healed by primary union. The toxins were begun shortly after operation and continued for six weeks longer. The patient was shown before the Clinical Congress of Surgeons of North America, in November 1912, at which time he was in perfect health with no trace of local or general recurrence. A second four weeks' course of treatment was given in December. (Patient was still perfectly well, in July, 1913.)

CASE 27. — *Myelo-sarcoma of the lower end of the tibia, twice recurrent; disappearance under eight months' treatment with the mixed toxins, patient now well eight years later.*

K. K., female, aged 21 years. Admitted to the Hospital for Ruptured and Crippled, September, 1904; operated upon October 11, by Dr. V. P. GIBNEY. The entire lower third of the tibia was involved, only a thin outer shell being left, as shown by X-ray photographs. A second operation was done January 5, 1905, consisting in the removal of a large mass of sarcomatous material with chisel and curette. At neither operation was any attempt made to remove the entire tumor. After the second operation the patient was put upon the mixed toxins and a few weeks later, the X-rays were given in addition to the toxins. At first there was some increase in size, but later, under large injections, followed by more severe reactions, the tumor was held in check and, finally, slowly receded. The treatment was continued until July, 1905, by which time the tumor seemed to have entirely disappeared. The patient has remained in perfect health without any sign of recurrence, up to the present time, or eight years after the treatment was begun. The microscopical examination in this case was made

by Dr. F. M. JEFFRIES, Professor of Pathology to the New-York Polyclinic. The patient was shown in perfect health before various medical meetings, the last, the Clinical Congress of Surgeons of North America, in November, 1912. My last examination was made December 2, 1913, and she was in good health with no recurrence, nine years later.

CASE 28 — *Osteosarcoma of the lower jaw. Periosteal origin. Combined treatment. Partial removal by operation followed by toxins. Complete recovery floor 8 months later from nephritis.*

C. J. V. W., male, 17 years of age. Family history good; no antecedent injury.

The patient was admitted to the General Memorial Hospital on January 10, 1910. Had always been in good health until the latter part of November, 1909, when he noticed an enlargement of his lower jaw, most marked in the region of the symphysis. The tumor grew very rapidly, extended on either side, and soon involved the floor of the mouth. There was no pain at any time. He was referred to me by Drs. BORST and SADLER of Poughkeepsie, N. Y.

Physical examination at the time of admission to the hospital showed a large tumor, $4\frac{1}{2}$ by $2\frac{1}{2}$ inches, smooth, symmetrical, occupying the entire lower portion of the jaw and extending back nearly to the angle on either side. There was also a tumor projecting downwards fully an inch beyond the normal outline of the bone. The mass in the floor of the mouth was continuous with the jaw and filled up the space nearly to the level of the teeth; the skin over the chin was normal and there was no evidence of ulceration in any part of the tumor. In consistence the tumor was very firm and hard, a typical osteosarcoma, causing very marked deformity due to the elongation of the chin.

Inasmuch as the only operation that could be performed with any hope of success would have been removal of almost the entire lower jaw as far back as the angle, it seemed to be wise to do a partial operation, to be immediately followed by the toxins. Therefore, on January 11th, with the assistance of Dr. DOWNES, I performed the following operation :

The lower lip was drawn forcibly downwards, without cutting it;

the mucous membrane on the inner side was then cut, exposing the outer portion of the tumor; the soft part were separated from the the tumor and by means of a chisel, the larger part of the external portion of the tumor was removed, a sufficient amount of alveolar process being left to hold the teeth firmly. The inner portion of the tumor, occupying the floor of the mouth, somewhat larger in size than an English walnut, was not touched at all. The tissues removed, macroscopically, were typical of osteosarcoma originating in the Periosteum. The report of the microscopical examination made by Dr. JAS. EWING, Professor of Pathology at Cornell University, read as follows: « Giant-celled osteosarcoma. It is not the ordinary encapsulated giant-celled sarcoma of the jaw or of the epulis type, but a tumor infiltrating in all directions, of rapid growth and with a large amount of new bone formation. »

Two days after the operation the patient was put upon small doses of the mixed toxins, given in the pectoral region. These injections were continued about four times during his five weeks' stay in the hospital, twenty-eight in all being given. Only three of these were made into the tumor in the floor of the mouth.

The patient then returned to his home in Poughkeepsie, where he was under the care of Drs. SALLIER and BORST, by whom the injections were continued three times a week, the highest dose given being five minims. Moderate reactions were obtained with an occasional chill followed by a temperature of 103° or 104°, but usually only by slight malaise and a temperature of 99° or 100°.

After the first three or four injections there was noticed a marked diminution in the size of the growth that had been left behind, both externally and internally, and when he left the hospital, the tumor in the floor of the mouth had diminished to one-third of its original size. Since then, the remainder of the tumor had nearly disappeared. The tumor tissue which was necessarily left behind externally also gradually became absorbed, and there was absolutely no deformity remaining.

Patient was shown before the New York, Surgical Society, on March 23, 1910, in perfect condition.

In April he developed a nephritis which, in spite of treatment, grew worse, finally causing death in August, 1910. There was no trace of a recurrence of the growth at the time of death.

It is possible that the continued severe reactions of the toxins exerted a causative influence in developing the nephritis. There have been two or three cases in my entire experience in which albuminuria was apparently caused by the toxins, but this, with two exceptions, was temporary only.

CASE 29. — *Spindle-celled sarcoma of the sternum, successfully treated with the mixed toxins of erysipelas and bacillus prodigiosus.*

Mrs G., 38 years of age (referred to me by Dr. DAVID JOHN of Yonkers). Mother died of tumor of the brain twelve years ago. Patient always in good health until June, 1906, when she noticed an enlargement of the upper portion of the sternum, especially marked over the sterno-clavicular joint on the right side. This slowly increased in size until December, 1906, when I first saw the patient. At that time there was a tumor the size of half an egg in the upper portion of the sternum, extending to the right over the sterno-clavicular articulation; consistence moderately soft, not fluctuating. I advised an exploratory operation to confirm the clinical diagnosis of sarcoma. This was performed by Dr. JOHN on December, 29, 1906 and the specimen removed was examined by Dr. JAS. EWING, Professor of pathology at Cornell University Medicine School, as also by Dr. B. H. BUXTON and Dr. MARTHA of the Loomis Laboratory, who pronounced it spindle-celled sarcoma. On January, 6, 1907 the mixed toxins were begun by Dr. JOHN under my direction, the initial dose being $\frac{1}{2}$ minim; this was gradually increased until by the end of the month 2 $\frac{1}{2}$ minims were reached which produced a temperature of 103 or 104°. After twenty injections had been given the tumor had considerably decreased in size and the treatment was discontinued for two weeks, during which time the tumor markedly increased in size again and a small lump appeared beneath the sterno-mastoid muscle. The injections were resumed and continued with occasional intervals of rest for nine months. At first the tumor above the clavicle increase under the treatment, but by the middle of June some breaking down was noticed in the sternal tumor followed by slight discharge of necrotic tumor tissue which continued for nearly six months. The tumors continued to steadily decrease in size after the treatment had been discontinued and the patient's general health improved.

The case is interesting from the fact that she received the largest doses directly into the tumor of any case in my experience, namely 30 minims. August 11, 1909, Dr. JOHN wrote : « She has had no apparent recurrence of the growth, but has very severe periodical headaches and her mental condition is not entirely normal ». On account of the severe pain from the tumor in the early of the disease, she became addicted to the use of alcohol to such an extent that it was impossible later to overcome the habit. On November 21, 1911, Dr. JOHN wrote : that her addiction to alcohol had increased so much that she became an inmate of the Long Island State Asylum in Brooklyn, and died a little later.

In regard to her tumor, the trouble which immediately concerns us, it appears that a large tumor of the sternum with metastases in the neck, the diagnosis of spindle-celled sarcoma confirmed by three pathologists, disappeared under prolonged toxin treatment and the patient was free from recurrence more than 5 years thereafter.

CASE 30. — *Inoperable round-celled sarcoma of the retroperitoneal region and ilium clinical diagnosis.*

J. G. K., male, 25 years of age. In December, 1911, first noticed swelling just above the crest of the ilium on the right side. This gradually increased in size but there was no pain; no swelling in leg; slight loss of weight. The patient was referred to me, March 26, 1912, by Dr. E. W. HEDGES of Plainfield, N. J. Physical examination at this time, showed a tumor behind the right inguinal and iliac region, extending down over the crest of the ilium, but not into Scarpa's triangle, and upwards, about three inches. It apparently had its origin in the retroperitoneal region, or anterior surface of the ilium the skin was not involved. The tumor was soft and semi-fluctuating with small areas almost nodular in character. Aspiration at various times showed only bloody serum.

The patient had been examined by Dr. JOHN L. ERDMAN (N. Y. City), who believed the trouble to be of malignant nature and inoperable. He was admitted to Dr. BULL's Private Hospital where the treatment with the mixed toxins was started, and continued for two months. At the end of four weeks the tumor became distinctly fluctuating, and under ether I made incision just above the upper part of the ilium;

and evacuated several ounces of fluid, with a large amount of necrotic material resembling brokendown sarcoma. The microscopical examination was negative as the material was too degenerated. The toxins were continued for several week longer. The sinus healed and the patient is at present in good condition one and a half year later.

CASE 31. — *Sarcoma of the humerus. Periosteals spindle celled.*

Mr. L., 35 years of age. No history of cancer in the family; a man of splendid physique, six feet tall, weighing 180 pounds. Early in January he fell and received a spiral fracture of the left humerus at

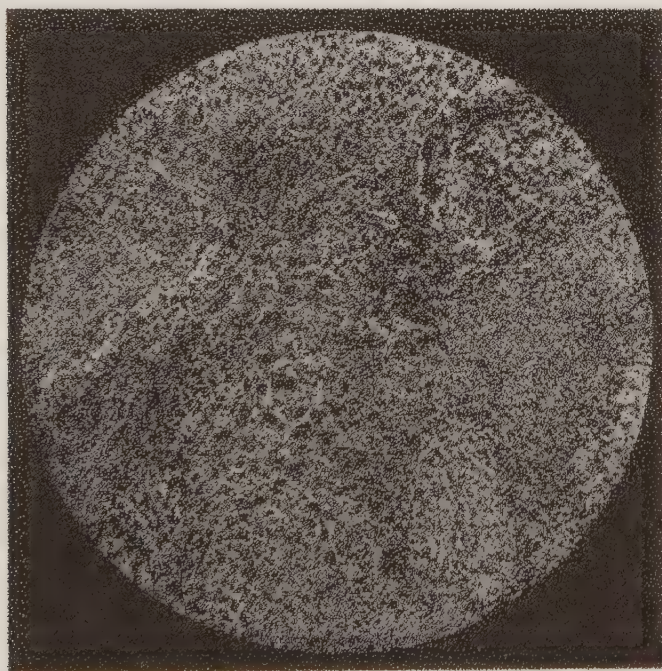


Fig. 3 (Case 31).

about the junction of the middle and upper thirds. He was treated at the Hudson Street Hospital, and then returned to Baltimore, where he was treated by Dr. W. A. FISHER. An X-ray taken at this time showed a spiral fracture without any trace whatever of a new growth.

Two to three weeks later he began to have severe pain at the site of the fracture. An other X-ray photograph was taken, showing that in the meantime there had developed a well-marked tumor, apparently a sarcoma, involving both the central portion and the periosteum. The growth increased rapidly in size, and was accompanied by very severe and constant pain.

In June, 1910, an exploratory operation was performed by Dr. J. M. T. FINNEY, who found a large sarcomatous growth involving both the central and periosteal portion of the humerus and extending from about the junction of the middle and upper thirds nearly to the head of the bone. The bone was completely destroyed; a pathological fracture had occurred and there was a flail joint. The central portion of the tumor was curetted; in Dr. FINNEY's opinion amputation offered no hope of a cure.

A few days later the patient was sent to me by Dr. FINNEY for the treatment with the mixed toxins. The treatment was begun on June 16, 1910, and continued in small doses, most of them being given systemically, in the pectoral region and a few in the arm. There were slow but steady decrease in the size of the tumor and immediate cessation of the pain, which had been constant from the first appearance of the tumor. The shell of bone about the tumor, which had undergone spontaneous fracture, gradually became harder with the formation of new bone, and within a few weeks complete union occurred. The large cavity gradually filled up with granulations. Several curettements showed the material to be sarcoma of the same type as the original tumor, namely, spindle-celled. The pathological examinations were made by J. C. BLOODGOOD of JOHN HOPKINS and also by JAMES EWING, Professor of Pathology at Cornell University Medical School. Dr. BLOODGOOD regarded it as a very malignant type of sarcoma which he characterized as « Bone aneurism ».

Another X-ray examination in the latter part of 1910 showed that the new growth had apparently entirely disappeared and there was firm union of the arm. The patient's general condition was excellent. In November, the granulations began to increase again in size, and in spite of curetting quickly recurred. An X-ray taken in December showed a small shadow starting in the periosteum, in the axillary region, and I finally decided, early in January, to do a shoulder-joint amputation. There was a very large recurrence under the pectoral

muscle six months later, which I removed and again the toxins were administered. I heard from him in November 1913 when he was in the best of health, more than tree years after the treatment was begun. When he was sent to me by Dr. FINNEY he stated it was too far advanced to give any hope from amputation, and without the toxins there can be little doubt the disease would have ended fatally within a few months.

CASE 32. — *Spindle-celled sarcoma of the metatarsal bone, several times recurrent in leg thigh and gluteal region. Final disappearance; patient well ten years.*

F. K., female, aged 16 years; had a fall in 1888, injuring right foot. Shortly there after two lumps appeared in the foot in the region of the injury and grew steadily until 1889. When the patient was operated upon by Dr. WILLIAM T. BULL, at the New York Hospital, the third and fourth metatarsal bones being removed. Three years later she received another injury to the foot, which was followed quickly by a recurrence. A second operation — Syme's amputation — was then performed by Dr. BULL. In 1893 she fell down stairs, injuring the stump; shortly afterwards a lump appeared at the outer aspect of the stump, which slowly increased in size. Very soon another tumor appeared in the popliteal space, which grew with great rapidity until December, 1893, when it had reached the size of a child's head, and was removed by Dr. BULL. The tumor in the stump was treated by Dr. BULL and myself with the mixed toxins of erysipelas in January, 1894, with the result that it entire by disappeared. One and a half years later there was a recurrence in the stump, as well as in the popliteal region, and in 1896 I did a high amputation just below the trochanter, which was again followed by recurrence in the gluteal region. This was partially removed by operation and the toxin treatment was resumed and continued with occasional intervals, for three years. The tumor disappeared and the patient remained well for ten ten years, when she was lost sight of.

CASE 33. — *Spindle-celled sarcoma of the scapular region involving large part of left half of the thoracic wall; entire disappearance under three months' treatment with the mixed toxins; patient well eighteen years.*

S. C., female, aged 16 years. The patient was admitted to the New York Cancer Hospital, June 20, 1894. The tumor had started in

the left scapular region, four months before, and had grown very rapidly until the time of admission; it measured thirteen inches vertically behind, and extended around beneath the axilla and to the sternum in front. The growth was fixed to the scapula and to the ribs, and probably originated in the soft parts, over the scapula; it was about 2 inches in thickness in its most protuberant part, the skin over it being normal and perfectly movable. The left arm was bound down by the new growth so that it could scarcely be raised to a horizontal position. The mixed, unfiltered toxins were injected locally into the scapular portion of the tumor and continued with intervals of one to two days for nearly four months. Immediate and very striking improvement followed; at the end of three weeks the arm could be raised to a vertical position. After three months' treatment the tumor had entirely disappeared by absorption only, without breaking down. There was no evidence of inflammatory, tuberculous or specific disease. The diagnosis of spindle-celled sarcoma was moreover confirmed by careful microscopic examination by Dr. H. T. BROOKS, Professor of Pathology at the Post-Graduate Hospital.

Subsequent history. — The patient has remained in good health up to the present time, nineteen years afterward. She was examined by my associate, Dr. D. H. M. GILLESPIE, a year ago, and he found no trace of a recurrence.

CASE 34. — *Sarcoma of sacrum, partial removal, followed by prolonged toxin treatment.*

D. C., male, 35 years of age; operated upon in the latter part of July, 1910 by Dr. WM. J. MAYO, of Rochester, Minn.

In a letter dated August 3, 1910, Dr. MAYO states :

I have just operated upon Mr. C. removing the coccyx and lowest sacral vertebra with the tumor which grew from the periosteum of the coccyx and fifth sacral vertebra. The sacral coccygeal juncture was penetrated by the growth and while the operation was an extensive one, I have no faith that it is curative and am sending him to you for treatment.

The patient consulted me on the 22nd of August, 1910, and the toxins were immediately begun and later continued by his family

physician at home. The pain which had been continuous since some time before the operation, gradually diminished and his general health improved. On March 22, 1911, when the patient reported to me again, I found his weight had increased from 118 to 145 lbs. There was some pain still, especially on sitting, but it was less than at the time the treatment was begun. I saw the patient again in the early part of 1912 and found his improvement had continued. His weight was normal and he stated that he had been able to perform his regular work ever since the treatment was begun.

The frequency of the injections was gradually lessened and in the summer, 1912, I advised discontinuing them altogether. More than two years, he remained in good health until the early part of October, 1912, when he found himself suddenly unable to empty either bladder or rectum. He again consulted Dr. W. J. MAYO who referred him to me. He consulted me on October 28, 1912. At this time he had been unable to pass water without a catheter for nearly four weeks and had no stools without an enema. His general health seemed good. I had another X-ray plate taken by Dr. B. C. DARLING who thought there was evidence of recurrence at the site of the old tumor. The patient was also carefully examined by Dr. PEARCE BAILEY who believed there was unquestionably a recurrence, pressing on the nerves supplying bladder and rectum, and advised resumption of the toxin treatment. I began at once with small doses, gradually increasing until a reaction temperature of 102 or 104° was obtained. He received from three to five injections a week. At the end of the first week a normal movement of the bowels occurred; but he was unable to pass any water until the end of four weeks' treatment when he passed a small amount. The injections were continued in large doses, in spite of some loss of weight. At the end of seven weeks I sent him home and advised two weeks' rest. The ability to pass water has been very slow in returning and, on January 22, 1913, he states that he still has to use the catheter, although he passes some water every day.

He adds :

I still feel fine, sleep fine and have a great appetite; have gained 8 lbs. take the treatments twice a week with very little reaction. Latest Report March 16, 1914, states « I five better those show for several years. »

This seems to be an exceedingly convincing case of the inhibitory action of the toxins, regardless of what the final outcome may be.

CASE 35. — *Sarcoma of the upper end of the tibia, central.*

C. M. R., female, 16 years; seen in consultation with Dr. IAVING, D. STEINHARDT, on April, 8, 1910. Family history : aunt died of cancer of the breast. Personal history : about six months ago first noticed pain in the region of the left knee, just below the joint. The pain was irregular, sharp and worse at night. There was no history of trauma. Physical examination showed slight swelling at the upper end of the left tibia; marked tenderness; semifluctuating on palpation; slight egg-shell crackling sensation; no lameness; no limitation of motion; no disability; the knee was slightly more painful after a long walk. The pain slowly but steadily increased, also the swelling. An X-ray photograph taken at the New York Hospital shows the typical appearance of sarcoma, apparently of central origin, in the upper end of the left tibia. I advised a conservative operation, curetting, to be immediately followed by a long course of the toxin treatment. Operation was done on April 10th, 1910. A typically sarcomatous tumor was found at the site of the swelling, occupying the central portion and extending nearly into the joint, but not involving it. The clinical diagnosis was confirmed by microscopical examination made at the Cornell Medical School Laboratory.

The patient made a good recovery, and the treatment was carried out under my direction by Dr. STEINHARDT.

In a letter received from Dr. STEINHARDT, dated September, 10, 1911, he states :

Following the operation done in April, 1910, the patient was put upon the mixed toxins, as suggested by you, the injections being given twice a week for a period three months, then once a week for one month. The patient improved and gained in weight. I last saw the patient in December 1910, when she was in remarkably good health.

A letter received from the father a few days ago states that she still continues to enjoy good health.

A letter received from the patient, January, 26, 1914, contains the information that she has been in good health up to the present time

and that there has been no return of the disease four years after treatment.

CASE 36. — *Sarcoma of the ilium (Clinical diagnosis only). Entire disappearance under the toxin treatment. Patient well at present, seven years later.*

N. G., male, aged 13. Family history : good. Past history : Fell downstairs two years ago 1904, striking left pelvic region; in bed about two weeks; fell again a year later, striking same side; laid up in bed for three weeks. Soon noticed some swelling in the region of the left ilium, which gradually increased in size; during last six months there has been some slight loss of flesh and decline in general health. Patient referred to me by Dr. LA FEATE, of Detroit, in August, 1906. Physical examination at this time showed a tumor involving almost the entire left ilium, being hard in some, and soft in other places; considerable limitation of motion in the left leg, marked loss of flexion of left thigh; he had some pain during last year, which at times was paroxysmal. The patient was admitted to the General Memorial Hospital in August, 1906, and put upon the mixed toxins; the treatment was continued for a little over a year, with two intervals of a few weeks' rest; highest dose, 8 minims. The injections were made into the buttocks. The swelling gradually decreased and limitation of motion nearly disappeared. At the end of a year the tumor had practically disappeared, although there remained some enlargement, apparently due to the new-bone formation, as often seen in osteo-sarcoma. The patient is still in good health at present 7 years later.

CASE 37. — *Recurrent spindle-celled sarcoma of the tibia; amputation advised by other surgeons; entire disappearance under four months' treatment with the toxins; patient well at present fourteen years after.*

W. F., male, 27 years old; Canadian; farmer by occupation. In March, 1897, patient noticed a swelling over the tibia of the left leg at about the junction of the middle and upper thirds; this slowly increased in size, and on July 28th he was operated upon by Dr. STEWART, of Toronto. The tumor recurred, and in November

25th, of the same year, a second operation was done, consisting in incision and curetting of the bone; some of the tissue was sent to Dr. JOHN CAVEN, Professor of Pathology at the University of Toronto, Canada, who pronounced it spindle-celled sarcoma. The tumor promptly reappeared, and the patient was referred to me for the toxins in February, 1899, by Dr. CAVEN.

Physical examination at that time showed a tumor at about the junction of the middle and upper thirds of the left tibia 3 by 4 inches in extent, with ill-defined border; over the central portion were two ulcerations, the size of a silver quarter. The patient was sent to the General Memorial Hospital and put upon the mixed toxins of erysipelas and bacillus prodigiosus for about two months. The tumor rapidly disappeared under the treatment; the bone cavity healed by healthy granulations. Before the healing process was entirely completed, the patient contracted a severe attack of accidental erysipelas (a fresh case of erysipelas had been in the ward not long before), running the usual course of about ten days. Healing continued rapidly and was completed two to three weeks later. The patient returned to his home in Chesley, Ontario. He has been in good health ever since, fourteen years later, and has been able to attend to his usual duties as a farmer.

He was shown at a clinic given at the time of the Clinical Congress of Surgeons of North America, in November, 1912, with a perfectly sound and useful leg.

CASE 38. — *Inoperable sarcoma of the spine involving the brain.*

Baby W., male, aged 2 years and 9 months, was brought to me in March, 1911, by his father, who is a physician in Virginia, with the following history :

In February, 1911, the father was thrown out of a wagon while holding the child in his arms. The spine of the latter was undoubtedly injured although nothing was noticed at the time. One month later, the child began to get weak, and in the latter part of March some swelling was noticed, situated two inches above the upper border of the clavicle, on the right side. This increased rapidly in size, and the patient continued to lose power of muscles. In the latter part of April, 1911, the father consulted

Dr. STUART MCGUIRE (Richmond, Va.), who believed the tumor had nothing to do with the trouble, which he pronounced infantile paralysis. No attempt at removal was made. The tumor apparently originated in the upper part of the spine. The patient could not move himself at all, neither could he hold up his head. There was marked muscular tremor of both hands, and almost entire loss of power in arms. The child kept growing steadily worse, and his father again brought him to Dr. MCGUIRE, who had a neurologist, Dr. H. ALLISON HODGES, to see the case with him. They both thought that the symptoms were due to cerebral disease, probably tuberculosis, but upon the father's request, Dr. MCGUIRE agreed to make an exploratory incision over the swelling in the back.

The lump was plainly palpable, and suggested the presence of a lipoma or collection broken-down tuberculous tissue. On exposing the growth, it was found to be a well-defined tumor springing from the laminae and transverse processes of the vertebrae. As the case was plainly inoperable, a piece of tissue was removed and the wound closed. Microscopical examination made by Dr. E. GUY HOPKINS, of Richmond (Professor of Pathology at the University College of Medicine) proved it to be fibro-sarcoma. The patient kept steadily growing worse after the operation, and Dr. MCGUIRE gave him but two months to live.

The toxin treatment was started in the latter part of July, 1911, under my advice beginning with $\frac{1}{5}$ minim, which gave a reaction temperature of 102. The highest dose injected systemically was 3 $\frac{1}{2}$ minims which caused a temperature of 103 $\frac{1}{2}$, the highest local dose was two minims. The child's weight steadily increased during the treatment, and in March, 1912, he weighed 29 pounds, a gain of eight pounds. He has regained considerable power, and can move both hands well, also can hold up his head, and can move both legs although he cannot walk with a support. Knee reflexes exaggerated; he has a good appetite. I made a physical examination of the patient in March, 1912, which showed, in the right side, two inches below the upper border of the clavicle, just to the right of the vertebral line, a scar, 4 inches long, running obliquely down and to the right. Slight fulness was noticed.

Dr. FOSTER KENNEDY, of New York City, also made a neurological

examination on the same day (March 19, 1912), and gave the following report :

On examination the child shows marked cerebellar attitude of the head, though the attitude referable to one lobe is not constant. Frequently there is a marked tremor of the head, precisely of the same character as that seen in advanced cases of disseminated sclerosis of the cerebellar or medullary type, or of advanced cases of Friedreich's ataxia. The pupils are brisk, the light and accommodation equal, central and regular in outline. There is no ptosis. There is marked nystagmus on lateral conjugate movement, either to the right or to the left. Query, weakness of the left sixth nerve. Jaw deviates always to the right, therefore query right motor fifth nerve affected. The masseter on the right side contracts less well than that on the left. Child apparently hears on both sides. There is obviously no defective vision, no changes in the sensibility of the face, nor is there any facial palsy. The tongue comes out straight, and there is no tremor, nor wasting. Palate normal.

Upper extremities. — There is marked motor ataxia in both arms of definitely cerebellar type. (N. B. This ataxia is not in any way dependent on any sensory defect.) Diadokokinesia right and left. The arms are very strong for all movements. There is no wasting, No paralysis in the legs. All movements can be performed, but the ataxia manifested in the arms is present in the lower limbs also. The sensory condition is everywhere normal, that is to say, the child appreciates pin prick, touch and temperature everywhere. There is no sequent of anaesthesia or hyperaesthesia in any way corresponding to the situation of the tumor in the mi-dorsal region.

Reflexes. — Arm jerks normal. Abdominal reflexes present, R. and L. and equal. Knee jerks increased equally, R. and L. Double extensor responses. Owing to inattention of the child combined with gross nystagmoid movement of the eye balls it was difficult to get a clear view of the optic discs. The veins in each ocular fundus were very large. Outer edge of discs were seen in glimpses and were apparently clear, and did not present the sinuosity of outline or the blurring usually seen after the subsidence of a neuritic process.

. We are told that the child has improved very greatly in the past six months not only as regards weight and general nutrition, but in regard to power and ability to perform movements. It is obvious, however, that there is still a gross cerebellar lesion.

Pathological examination made by Dr. JAMES EWING, March, 29, 1912, whose report reads as follows :

In the case of Baby W. I am unable to offer a positive and exact diagnosis. It is certain that you deal with a malignant tumor which may very well be called sarcoma. I am inclined to think it is either an endothelioma secondary to the cerebral growth, or possibly a neurocytoma derived from misplaced nerve tissue in the cranium.

Under date of November 23, 1912, the patient's father writes :

In reply to your letter, I am glad to say that the little boy's condition has improved some since you saw him in March. There is no indication of the return of the growth that was on his back. He has never regained the use of his legs, though he can move them better, and they show no signs of wasting nor of contractions. His eye symptoms are also better, and he is hearty and well developed, does not seem to suffer any, and is bright and full of life.

I let him rest from the toxins from October 1st to November 15th and now I give him a dose three times a week.

From his symptoms there must be some pressure about the base of his brain you remember Dr. KENNEDY thought so too. I would like to have Dr. HARVIE CUSHING examine him, but it is a long trip, and I do not know that I could consent to an operation just now if he was to advise it. He seems to improve slowly on the toxins, and if the pressure of the brain is caused by a similar growth to the one that was on his back, I don't know if an operation would be advisable. His trouble might be due to metastasis. The toxins have certainly saved my boy's life and I am deeply grateful for what you have done.

A more recent letter received from the child's father, under date of July 23, 1913, states :

Am glad to say that my little boy's condition is somewhat improved. He cannot use his legs but little; he can move them, but has no strength in his knees. There is no signs of a return of the growth on his back, and his general health is good; his mind seems bright. I give him four minims of the toxins about every third day.

Subsequent history. — The toxin treatment has been continued by the father, with occasional intervals of rest up until the present time. Although the child has not completely regained his functions, the tumor of the spine has apparently disappeared, and there has been

no sign of a recurrence now, two years afterward. In view of the rapid growth of the tumor, and the fact that its malignancy was established by microscopical examination, the inhibitory effect of the toxins in this case is very striking.

CASE 39. — *Round-celled (giant-celled) sarcoma of the sternum with metastases in both cervical regions.*

Miss C., aged 19 years; family history negative. Patient had an attack of typhoid fever in 1912, which confined her to bed for two or three months. In the early part of January, 1912, during convalescence, she noticed a small lump over the left outer margin of the manubrium, about the junction of the second rib. This increased rather rapidly in size, and then diminished considerably, after which it again began to increase, and was associated with constant pain of a throbbing character; no temperature. There was local redness and marked tenderness, also semi-fluctuating « feel » to palpation. Patient at this time came under the care of Dr. W. L. PERLE, of Richmond, Va., who after a clinical examination regarded the case as either inflammatory tumor of typhoid origin, or sarcoma. Operation revealed a mass with the characteristic « eels meat » appearance, but not infiltrating the surrounding tissues. It was easily shelled out. The outer plate of the manubrium was eroded away, the area being about the size of a silver quarter; free hemorrhage followed, which necessitated packing.

Microscopical examination was made by Dr. E. GUY HOPKINS, of Richmond, whose diagnosis was : « Giant-celled sarcoma (myeloma developing from the marrow of the bone. »

In November 1912, the mixed toxin treatment was started by Dr. PERLE, who began with $\frac{1}{3}$ minim and increased until a decided reaction was obtained; the maximum dose being 3 minims.

Later the patient's susceptibility increased so that one minim produced a marked reaction. About the middle of January, 1913, local redness was noticed which grew rapidly. The patient was then seen by Dr. GEORGE BEN JOHNSTON of Richmond, Va., who later referred her to me.

Physical examination at this time showed the upper third of the sternum occupied by a tumor, extending over the whole width of the

sternum, and from the upper portion downward 2 and $\frac{1}{2}$ inches. It was smooth and globular, projecting 1 and $\frac{1}{2}$ inch. The skin was purplish red in color, and ulcerated over an area the size of a silver quarter. Typical appearance of rapidly growing round-celled sarcoma. Patient's general health was good. She then came to New-York to be under my care, and entered the hospital (middle of February, 1913) for further toxin treatment. The second physical examination showed very marked increase in the size of the growth since my examination made in Richmond on February 8th. During the past week the glands had become markedly enlarged on both sides of the neck, as well as in the supraclavicular and mid-cervical regions, the swelling being more pronounced on the right side than on the left. The tumor itself had also increased markedly in size, and in projection. The ulcerated area had become enlarged, and assumed a fluctuating appearance. The general condition of the patient was much weaker, and she had lost considerably flesh. The disease proved to be evidently of an extremely malignant character. Interstitial injections of the toxins were made in the pectoral region. The patient was very susceptible, and small doses produced a temperature of 102 to 104°. Three minims was the highest dose she could stand. Treatment was continued for four weeks, with apparently no effect in checking the progress of the disease. A specimen was removed under cocaine, and was sent to Dr. EWING, on March 14, 1913; the latter however was unable to make positive diagnosis of any sort owing to its broken-down condition.

The patient then returned home where Dr. E. D. RELLINS (Gate City, Va.) continued with the toxins merely for the moral effect. He states that after she reached home she gained some in weight and he then started her on full doses of the toxins every other day, which seemed for a time to check the course. After a short time the disease progressed very rapidly under the continued use of the toxins, and he expected her death at any time on account of some severe hemorrhages. However, Dr. ROLLINS later states that, "for the past two months (June and July) the glandular enlargement has disappeared, the pain has ceased, and the patient has had no morphine for six weeks; also the drainage from the tumor has practically ceased, and but for some nausea and vomiting, she rests as if there were no trouble. I am still giving the toxins every second or

third day; it requires a much smaller dose now to cause a reaction ».

· In a letter received from Dr. RELLINS, under date of September 16, 1913, he states : « I have been waiting too see the final outcome in the case, before making a report to you, which report, it looked would be a cure, but, two weeks ago oedema showed up (of nephritic origin) and she died, September 12, 1913. The tumor had gradually sloughed, and was nearly on a level, and had healed a strip $\frac{1}{2}$ inch. The glandular involvement had disappeared. If the favorable turn had taken place while her general condition was fairly good, she would have had, I think, a nice recovery ».

· This case is of very great interest, inasmuch as improvement did not occur until the toxins had been used for several months, and then the patient's condition was regarded as absolutely hopeless, and death was expected in a short time. Then, unexpectedly, the growth began to diminish in size; the metastatic tumors entirely disappeared and the primary tumor had practically gone when the kidney complication developed.

· Another feature of great interest is, that, here we have a giant-celled sarcoma or myeloma (at least so called by the pathologist), of a slight degree of malignancy, associated with extensive glandular metastasis. This is contrary to the opinion held by BLOODGOOD and others that giant-celled sarcoma never produces metastasis.

CASE 40. — *Periosteal sarcoma of the femur. Complete disappearance, followed by metastases a year later and death within a few months.*

H. K., male, 10 years of age. Patient was admitted to the Hospital for Ruptured and Crippled in November, 1906, with a history of having had occasional pain in the left leg for several months. In July, 1906, the pain became so severe that he was kept awake nights. This was followed by falling off in general health. The patient was treated first for rheumatism, and later for periostitis. In September, 1906, a fusiform enlargement was noticed in the middle of the left femur. Patient was then admitted to the hospital with a diagnosis of periostitis made from the clinical and X-ray examinations. The latter showed nothing characteristic, except a tickening apparently outside of the bone, in the periosteum. Physical examination at that time showed a fusiform enlargement of the entire left

femur, 6 $\frac{1}{2}$ inches in length, reaching within 2 $\frac{1}{2}$ inches of either extremity. After a careful examination I made a diagnosis of periosteal sarcoma, which was later confirmed by an exploratory incision under ether, November 26, 1906. The tumor was found starting in the periosteum, apparently surrounding the entire bone, about one-half inch in thickness over the most prominent part. A portion was removed for microscopical examination, which was made by Dr. JEFFRIES, the pathologist of the hospital, professor of pathology on the New-York Polyclinic Hospital, who pronounced it small round-celled sarcoma.

The patient was put upon the mixed toxins, January 28, 1907, at which time the tumor over the central portion measured 11 $\frac{3}{4}$ inches. The toxins were slowly increased from $\frac{1}{2}$ to 11 minims, injected chiefly into the tumor itself. The central portion of the tumor began to slowly decrease in size until it measured only 10 $\frac{7}{8}$ inches. The doses were then increased up to 7 minims, whereupon the tumor diminished in size until it measured 9 $\frac{15}{16}$ inches. He showed slight loss of weight while the large doses of the toxins were being given, his lowest weight being 45 $\frac{1}{2}$ lbs. which was 4 $\frac{1}{2}$ lbs. less than when the treatment was first started. He received in all fifty-seven injections. The tumor of the femur had become almost completely under control and by September, 1907, nearly a year later, it had entirely disappeared.

Subsequent History. — Shortly after metastatic tumors began to develop in the region of both orbits, and death occurred a few months later.

In this case a rapidly growing and highly malignant periosteal sarcoma of the femur, disappeared under the toxin treatment alone, and the subsequent metastases a year later proved the correctness of the diagnosis.

CASE 40. — *Periosteal round-celled sarcoma of the skull and forehead.*
(Clinical diagnosis only).

Mr. T., 60 years of age, was referred to me in April, 1907, by Dr. A. T. BRISTOW of Brooklyn, N. Y.

Family history : Three brothers died of tumors of the abdomen presumably cancer.

Personal history : In December, 1906, she struck her head against a sharp corner of a bureau, causing some pain and soreness, but thought nothing more of it until two or three weeks later, when she noticed a hard enlargement of the point of injury. This slowly increased in size, until April 1907, when she was referred to me for an opinion. Examination at this time showed, in the forehead, just to the right of the median line and below the hair line, a hard swelling, apparently of periosteal or bony origin, firmly fixed, about $\frac{3}{4}$ of 1 inch in diameter and projecting beyond the surface about $\frac{1}{2}$ inch. I fully concurred in Dr. BRISTOW's diagnosis of sarcoma, and advised the use of the mixed toxins. The treatment was given Dr. BRISTOW three to four times a week from April to July, when she returned to her home in New York and the treatment was continued by Dr. SATTERWHITE under my direction. She received in all fifteen injections, and by the end of August, the tumor had entirely disappeared. I examined the patient on January 23, 1914, and found her to be in perfect condition with no sign of a recurrence. Eight years later.

CASE 41. — *Extensive periosteal round celled sarcoma of the femur, involving lower two thirds of the shaft with extensive multiple metastasis; cured with the mixed toxins, well ten years. A sarcomatous and epithelial tumor developing at the site of an X-ray dermatitis of thigh ten and-a-half years later; amputation; metastases; death in four months.*

CASE XX. — A. G., male, 18 years old. Microscopical examination by Dr. E. K. DUNHAM, Professor of Pathology at Bellevue Medical School and Dr. B. H. BUXTON, Professor of Experimental Pathology at Cornell University Medical School, showed it to be small round-celled sarcoma. Amputation at the hip-joint was strongly advised but refused by the patient and his family. Prolonged X-ray treatment started in February, 1902; retardation of the growth, but six months later he developed extensive metastases in the pectoral and ileolumbar region, involving the ilium. The pectoral mass was partially removed and proved to be a typical round-celled sarcoma. The tumor in the ileolumbar region was the size of a child's head, and was regarded as entirely inoperable. The patient was put upon the mixed toxins and

in four weeks the ileo-lumbar tumor became necrotic. The incision was made through the ilium and drainage established. Entire disappearance, no trace of any recurrence, ten and-a-half years later. Patient shown before the New-York, Surgical Society, April 1912.

The patient developed an epithelioma the size of a hickory nut in the pectoral region at the site of an X-ray dermatitis, in April, 1912, and in October, 1912, developed a very large and rapidly growing malignant tumor (epithelioma and sarcoma) at the site of an old X-ray dermatitis of the thigh. Rapid extension; amputation; lung metastasis; death January 15, 1913, four months from beginning of the epithelioma of thigh. It is the only case of periosteal sarcoma with metastases ever cured by any method of treatment.

Cass 42. — *Periosteal sarcoma of femur (clinical diagnosis).*

Mrs. G. M., right 27 years of age; in May, 1912, first noticed pain in leg, which was treated for rheumatism for two months, without improvement. There was 14 pounds loss in weight. An X-ray was taken and on basis of same a diagnosis of periosteal sarcoma was made and immediate amputation was strongly urged, without any further examination. The patient was two months pregnant, and in preparing for the amputation the uterus was emptied. Her husband was told that there was no possible alternative to amputation. The patient was referred to me on September 19, 1912. Examination at this time showed a hard, fusiform enlargement 7 by 8 inches in length, apparently of bony origin in the upper and middle thirds of the femur, gradually shading off into the normal outline of the bone. Largest circumference 19 $\frac{1}{2}$ inches; skin normal; no enlarged veins.

The patient entered the General Memorial Hospital and was put upon the mixed toxins. WASSERMANN examination of the blood proved negative. At the end of a week I made an exploratory incision in about the middle of the tumor, and on cutting down found a fusiform enlargement of the femur of the consistence of a periosteal sarcoma. The tumor extended about $\frac{1}{2}$ inch beyond the normal line of the bone. A wedgeshaped portion was removed; there was no trace of any inflammatory exudate and no infiltration of the surrounding tissues. Clinically it had the typical appearance of a periosteal

sarcoma, originating in the shaft of the bone, and the consistence and gross appearance of the specimen confirmed this view. The specimen was sent to Dr. EWING, who reported as follows:

September 28, 1912: The tissue shows very little if any specific process and does not permit of a diagnosis. There is infiltration of the vessels with large round cells, suggesting sarcoma, but which might very well be tuberculous. I ought not to express any opinion on the data received and I would not amputate without further information.

On entrance to the hospital, the measurements over the upper, middle, and lower part of the cicatrix, representing the upper, middle, and lower end of the original tumor, were as follows:

Right, 16 in.; 18 $\frac{1}{2}$ in.; 19 $\frac{1}{2}$ in. Left, 15 $\frac{1}{2}$ in.; 17 $\frac{1}{2}$ in.; 18 $\frac{1}{4}$ in.

November 7, right, 14 $\frac{1}{2}$ in.; 16 $\frac{1}{2}$ in.; 17 $\frac{3}{4}$ in. Left, 14 $\frac{1}{2}$ in.; 16 $\frac{3}{4}$ in.; 18 in.

November 26, right, 14 $\frac{3}{4}$ in.; 16 $\frac{3}{4}$ in.; 18 $\frac{1}{4}$ in.

The toxins were continued four to five times a week and the dose gradually increased from 0.5 minim to 6 minims. At the end of two weeks there was marked diminution in the circumference of the thigh. In view of the lack of certainty of Dr. EWING'S diagnosis and the rapid improvement under the toxin treatment, it was deemed very important to make a second exploratory incision, and on November 1 I made another incision $\frac{1}{2}$ inch away from the first, 5 inches in length, and cut down upon the tumor. The latter was found considerably smaller in size, projecting only about $\frac{1}{4}$ inch from the shaft of the bone. An opening was chiseled into the central portion of the bone and several pieces of periosteal as well as central growth were removed and sent to Dr. EWING. Clinically the tumor had every appearance of a partially necrotic sarcoma, a condition frequently seen as a result of the use of the toxins. Three X-ray photographs have been taken since by Drs. L. G. COLE and HOLDING, who believed the condition to be periosteal sarcoma. Dr. EWING'S report of the second specimen, dated November 1, 1912, reads:

Five sections from five different parts of the tissue received fail to show any signs of sarcoma. There is suppurative inflammation in an



Fig. 4 (Case 42).

area lined with granulation tissue. The periosteum and bone show an active productive and rarefying osteitis. I find no signs of syphilis or tubercle. The condition suggests to me a pyogenic infection of the periosteum or osteomyelitis.

The clinical history and macroscopic appearance at the time of operation make it impossible to regard it as an osteomyelitis.

Subsequent history. — The tumor slowly subsided under the toxin treatment and at the end of six weeks the circumference of the thigh became nearly normal. The patient had the toxins continued at home for the reason that I did not believe it wise to place too implicit faith in a negative pathological report from small portions of material removed at an exploratory operation. She had gained 10 pounds in weight.

January 6, 1913, examination shows the tumor has been increasing in size the last three weeks, but the general health is still good. I still believe the condition to be periosteal sarcoma.

NOTE. — February 16, 1913. Under larger and more frequent doses of the toxins the tumor is again decreasing in size.

Physical examination. — July 1, 1913, showed the measurements of the right thigh over the upper, middle and lower end of the scar (same region as measured before) 21, 20, 19 inches, left side, the same. Present weight 139 pounds. Patient has gained a pound a week since she left the hospital. The last X-ray taken a few months ago showed the bone apparently much more dense than at earlier sittings, as though the tumor tissue had been replaced by normal bone. General condition a present, perfect; no pain.

The X-ray photographs with the Clinical History strongly confirm the diagnose of periosteal sarcoma.

The toxins were kept up until the latter part of 1913 two to three times a week in doses up to 12 minims which gave moderate reactions; all injections were given systemically. The patient has gained steadily in weight and the last X-ray photograph taken January, 5, 1914, by Dr. DARLING, showed very little change from the one taken in July. The density of the bone seemed to have increased without any evidence of increase in size. As the sinus persisted, I

Fig. 5 (Case 42).

determined to enlarge it to see if a piece of dead bone might not be the cause of its failure to heal. Under ether anesthesia, a free incision was made down to the bone and the small opening which had been made during the earlier incision in the bone itself, was enlarged and curettings were taken from the interior of the bone and cicatricial tissue about the sinus removed for microscopical examination. The bone itself showed no evidence of tumor formation; it was somewhat denser than normal bone. The wound was closed by drainage, Careful microscopical examination of the tissues was made by EWING, whose report reads :

January 6, 1914.

The tissues in the case of Mrs. M. fail to show any definite evidence of a tumor. They represent dense fibrous tissue, the vessels of which are sheathed by numerous plasma cells. It is possible that these cells are a derivative of a perforating marrow tumor of the type of multiple myeloma, but the appearance is more suggestive of chronic inflammation. The wall of the sinus is lined by cellular and edematous granulation tissue.

J. EWING.

The typical clinical picture at the beginning, the marked improvement under the toxins, followed by increased growth, after the treatment was stopped, again followed by improvement on resumption of treatment and final recovery of normal health, leaves little ground for doubting the correctness of the clinical diagnosis of periosteal sarcoma, and the X-ray picture furnishes strong confirmatory evidence. March 10, 1914, patient in good health.

Were there no other cases of periosteal sarcoma on record in which a similar result had occurred, the diagnosis could not be accepted too implicitly without confirmation by microscopical examination. However, in case No. 41 a much larger periosteal tumor of the femur, with extensive metastases did completely disappear under the toxins, and the patient remained well for ten years. In this case the diagnosis was confirmed by microscopical examination made by Dr. E. K. DUNHAM, Professor of Pathology at Bellevue University Medicine School, and Dr. B. H. BUXTON of Cornell medical school.



Fig. 6 Case 42).

CASE 43. — *Sarcoma of the spine, spindle-celled.*

Mr. S., 44 years of age, referred to me in 1894, for an inoperable, recurrent sarcoma of the spine which had been pronounced spindle-celled sarcoma on microscopical examination. She was immediately put upon the toxins, the injections being made partly into the tumor, partly remote from it and continued for two months, with the result that the tumor entirely disappeared. The patient was reported well eight years later.

CASE 44. — *Very extensive round-celled sarcoma of the dorsal and lumbar spine; with paralysis of bladder and rectum and lower extremities; had lost 50 pounds in weight. Entire disappearance under injections of the mixed toxins of erysipelas and bacillus prodigiosus (no other treatment). Patient well eleven years.*

D. G., 21 years, entered Montefiore Home for incurables April 1904, at which time a large swelling was noticed in the back and lower dorsal region; patient unable to walk, but no paralysis of the leg. About six months after, a tumor was noticed on either side of the spinous process and lower dorsal- and upper lumbar regions, which gradually increased in size until February 18, 1902, when it was exceedingly large, and involved all the vertebra from the eighth dorsal to the third lumbar; muscles of the thigh were markedly atrophied and there was great general emaciation, total paralysis of bladder and rectum, and the patient was unable to turn over in bed; he had lost 50 pounds in weight. I was called in to see the patient by Dr. V.-P. GIANEX, who regarded him as entirely hopeless, and the diagnosis had been confirmed by an exploratory operation, and microscopical examination by Dr. HANLOW BROOKS, Pathologist to Bellevue Hospital. The toxins were begun with little hope of giving more than temporary relief. The treatment was carried out by Dr. WACHSMAN under my direction. The injections were made into the buttocks and pushed to the point of producing a moderate reaction a temperature of 103 or 104. Improvement was almost immediately noticed and steadily continued. By the end of September, 1902, the patient's general condition had markedly improved, and the tumor had consi-

derably decreased in size. The total paralysis was replaced by fair motive power and ability to walk; reflexes had reached their normal condition, and the area of sensory disturbances had diminished in extent and intensity. There was still some retention of urine, and some constipation. Dr. GIBNEY applied a plaster jacket which patient wore for a number of months; improvement went on until early

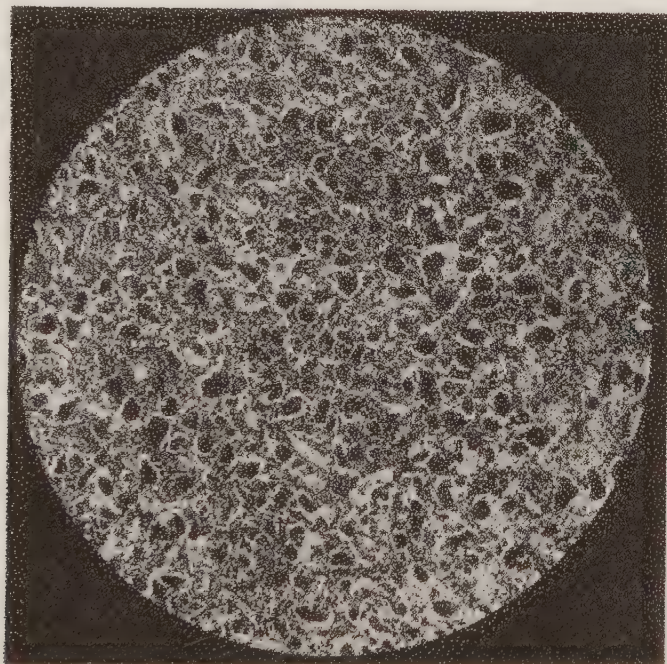


Fig. 7 (Case 44).

in 1903 when he had entirely recovered and the plaster jacket was discontinued. He resumed his regular occupation and has been working ever since and is in good health at present 12 years later.

A letter received from the patient August 10, 1912, states as follows:

« I know you would be surprised to see my improved condition. The last two and a half years I am working every day, and physical hard work, but I am feeling strong and my general condition is better than I ever dared to expect.

I weigh 145 lbs; the muscular development of my chest, arms,

shoulders and stomach is wonderful to what it was even three years after my sickness when I weighed but 95 lbs. My boys, one six, and one four, are in the best of health. »

CASE 45. — *Sarcoma of the scapula, inoperable without complete removal of the scapula and upper extremity; clinical diagnosis alone no microscopical examination in this case. — Patient well three years later.*

D. N., 2 months old; tumor developed shortly after birth; rapid growth; Physical examination on June 20, 1910, showed a tumor of bony origin, occupying nearly the entire posterior portion of the left scapula, of firm consistence, veins dilated, whole clinical appearance typical of sarcoma; while no specimen was removed for microscopical examination (I believed the Prognosis hopeless) the diagnosis was confirmed by Dr. V. P. GIBNEY who saw the child in consultation, The toxin treatment was started, the initial dose being $\frac{1}{10}$ minim which was gradually increased to 5 m^{m} which was the highest dose given. After four weeks treatment by me, the injections were continued by the family physician, Dr. JOHN HARRISON of Stamford, Ct., for nearly a year; constant but slow improvement followed and finally complete disappearance of the tumor, patient in good health at present three and-a-half years later; and was shown before the Clinical Congress of Surgeons of North America, November 12, 1912.

CASE 46. — *Giant-celled sarcoma of the upper jaw.*

E. S., 8 years of age. The patient came under Dr. James Mc LEON's (Buffalo, N. Y.) care in the summer of 1908, and the latter curetted out the tumor, which was not, however, thought to have been entirely removed. The patient was therefore referred to me by Dr. James McLEON for the mixed toxin treatment in September, 1909. Examination at this time showed three teeth, as well as a portion of the alveolar process, absent in the right superior maxilla. The wound from the recent operation had entirely healed but there was considerable thickening which, apparently, was sarcomatous tissue. I advised the toxins to be given in small doses and kept up for three or four

months. The treatment was carried out by Dr. McLEOD. The patient proved very susceptible to the toxins and the reactions were quite severe, the temperature in some instances rising to 105°.

Under date of March 29, 1911, *i. e.*, nearly two years after the treatment was begun, Dr. McLEOD writes that the boy has done well and that there is no sign of a recurrence.

October, 1913, Dr. McCLEOD writes :

There is no sign of a recurrence four years after treatment.

CASE 47. — *Inoperable sarcoma of the sacrum. Clinical diagnosis, entire disappearance under toxin treatment patient well seventeen years after.*

H. B. H., male, 38 years old. In February, 1895, the patient began to lose flesh and strength; soon after had pain in the lower part of the spine over the sacrum, the pain extending down the legs, more marked on the right side; he consulted Dr. W. C. DEMING, of Westchester, in April, 1895. At this time he had slight lameness of the left leg. All symptoms progressively increased, the pain becoming very acute, so much so that the patient wished to die. On May 2nd, he was sent to St. Lukes's Hospital, service of Dr. FRANCIS P. KINNICUTT. His normal weight of 175 pounds, had fallen to 134 pounds, and he could walk with the greatest difficulty. Careful examination of the rectum at this time showed a large, hard, tumor, attached to the anterior portion of the sacrum, the lower border of which could be reached by the index finger. The tumor was of firm consistence and very firmly fixed; its upper outline could not be determined. The diagnosis of Dr. KINNICUTT as well as that of the other attending physicians and surgeons who saw him in consultation, was inoperable sarcoma of the sacrum and pelvis.

I saw the patient in consultation on May 10, 1895, and advise a trial with the toxins for two to three weeks, to be then discontinued if no improvement was noticed. The injections were made directly into the buttocks and repeated daily. At the end of one week the pain had almost entirely subsided, and the lameness was much improved. The improvement continued rapid and constant; at the end of six weeks he returned to his home, where continued for some time, two to three

injections a week being given by Dr DEXING in the evenings so as not to interfere with his regular occupation, which he had resumed. At the end of seven weeks the patient had gained twenty-eight pounds in weight and stated that he felt as well as ever. Two years later his weight was 176 pounds. Seventeen years later he was in good health which resulted in his death which occurred at Harlem Hospital, New York.

In November 1912, he received an injury in an accident, until.

Series III cases of sarcoma originating in other structures those
Bone of glands.

CASE 48. — *Sarcoma intra-abdominal involving omentum, mesentery
of small intestine and gall bladder.*

E. J., 23 years old, female. In 1894 began to have attacks of pain in the right hypochondriac region, which gradually became more frequent and severe, with depreciation of general health until finally she was confined to bed. August 16, 1894 exploratory operation by Dr. WILLY MEYER of New York. A solid tumor was found apparently springing from the mesentery of the intestine and attached to omentum and gall-bladder. It was clearly inoperable and no attempt was made to remove it; a portion was excised for microscopical examination and the abdomen closed. The examination of the piece removed was made by the pathologist of the German Hospital, Dr. F. SCHWYZER, who pronounced it round-celled sarcoma.

Dr. Meven in his letter describing the operation, stated as follows :

At the physical examination previous to operation, in August, 1894, there was a small, irregular swelling on the outer side of the right rectus muscle about two fingers' widths above McBurney's point. On entering the abdominal cavity, I found a hard, irregular infiltration which involved the omentum, ascending colon, loop of small intestine, and the border of the liver, matting together all these parts. Clinically the disease impressed me, as also everybody present, as a malignant growth, probably sarcoma. To define clearly its origin was impossible; it seemed to start from the omentum, as this was especially involved. To remove the growth radically, seemed impossible. I also had not the permission of the relatives of the patient to do any major perhaps here fatal-operation which latter, in order to be radical,

would have had to consist in a resection of a portion of the large as well as of the small intestine, as also of a portion of the liver besides the omentum. I therefore removed a wedge-shaped piece of the growth for microscopic examination and closed the wound in the tumor by two catgut stitches. I regret now not having palpated at that time the gall-bladder, but a primary disease of the latter, probably due to the presence of gall-stones, did not enter my mind at all. Microscopic examination of the piece removed was made by the pathologist of the German Hospital, Dr. F. SCHWYZER, who pronounced it to be round celled sarcoma. Permit me to congratulate you on the outcome of this very interesting and important case.

Early in 1894, as soon as the patient recovered from the operation Dr. MEYER referred her to me for the toxin treatment. Palpation at this time showed an intraabdominal mass beneath the cicatrix in the right hypochondrium, about 4 inches in diameter; the tumor was hard and fixed. General condition good. Systemic treatment with the mixed toxins was begun, the injections being given alternately in the abdominal wall and buttocks. They were kept up, with occasional intervals of rest, until February 7, 1895 — five months, with the result that the tumor gradually disappeared. The patient was in good health and free from recurrence twelve years later since which time I have lost sight of her.

CASE 49. — *Round celled sarcoma of the iliac fossa;
nearly complete disappearance.*

Mr. R.; 55 years of age. Patient was admitted to the New York Cancer Hospital in June, 1893, with a tumor (said to have started in January 1893) about the size of two fists deeply seated in the right iliac fossa. There was marked pulsation, which was regarded as transmitted, and the tumor was diagnosticated as sarcoma. A portion was removed by exploratory incision, and the diagnosis confirmed by microscopical examination by Dr. E. K. DUNHAM, pathologist to the hospital.

Injectons of the erysipelas and prodigious toxins were at once begun, and continued with occasional intervals for the greater part of the entire year. The tumor almost completely disappeared under the treatment, and the patient was in good health one year after, beyond which time I was unable to trace hint.

CASE 50. — *Spindle-celled sarcoma of chest wall; soft parts; eight times recurrent—well at present 19 years later.*

Dr. X., 37 years of age. Very vascular, multiple tumors which, on microscopical examination proved to be spindle-celled sarcoma, extensively mixed with round cells. Examination showed the whole anterior portion of the chest covered with scars and recurrent tumors. The toxins were begun November 4, 1894 and continued in small doses with intervals of rest for three-and-a-half years. Two or three small nodules were removed in November, 1902, which, microscopical examination still showed them to be spindle-celled sarcoma insert Dr. Blt report, The toxins were again resumed for another period in small doses, not sufficient to interfere with his work. His general health continued good and weight normal.

A small apparently cicatricial nodule that had been present all along, began to increase in size in the beginning of June, 1911. I removed it under ether, and Dr. SOAMES EWING's report on the specimen reads as follows :

The tumor proves to be a myxosarcoma. It is almost cartilaginous in places. Most of it is not very cellular, but along the edges it is infiltrating the muscle tissue and hence is locally malignant. These tumors recur locally with persistence, but do not often involve lymph nodes or generalize.

The patient then started the filtered toxins and continued them, with occasional intervals of rest, for nearly a year, in doses not sufficient to cause any severe reactions or to interfere with his work. He is a very prominent surgeon of Greater New York, and is at present July, 1913, in good health and there is no evidence of any return of the disease nineteen years later.

Dr. GEO. P. BIGG' (Pathologist, New York Hospital) report, September 29, 1902, states :

The tumor from the chest wall measures $2\frac{1}{2} \times 2 \times 1$ centimetres. Through rather sharply outlined, it is not encapsulated. On microscopical examination it proves to be a sarcoma in which ovoid and spindle cells distinctly predominate though there are also round cells in moderate number. Fibrous stroma is much more abundant than is

usually the case in sarcomata, and in places it gives to the tissue the structure of a fibro-sarcoma. Invasion of muscle is shown at the periphery. The vascular supply is fairly abundant.

NOTE. — Another small nodule was removed March 12, 1914 from the same region, microscopical examination by Dr. EWING showed it to be of similar structure the toxins have been resumed in small doses.

CASE 51. — *Recurrent spindle-celled sarcoma of the palm of the hand entire disappearance; recurrence two years later, which proved fatal.*

Miss M., 18 years of age; had received an injury to her right hand in 1893. Two years later, in July, 1895, she noticed a small swelling in the palm of the right and, one half the size of a hickory nut which was removed by operation. The tumor recurred quickly and a second operation was done by Dr. EDW. MARTIN, of Philadelphia, on January 2, 1896. Microscopical examination showed the tumor to be a spindle-celled sarcoma. The tumor again recurred and on February 15, 1896, the patient was referred to me for a trial with the toxin treatment before resorting to amputation. The filtered preparation was used, later the unfiltered solution. Rapid and continued regression of the tumor followed.

On May 15, 1896, the tumor had entirely disappeared, and I presented the case before the American Surgeons Society, May 27, 1896. Most of the injections in this case were given systemically into the upper arm, in doses as large as 20 minims of the filtered preparation. The tumor recurred locally the two years later and failed to yield to further treatment. I advised amputation which was refused. She tried Christian science for seven months, under which the tumor grew to the size of a coconut. I subsequently amputated the arm, but the patient died a few months later from generalization.

CASE 52. — *Spindle celled sarcoma of palm of hand, six times recurrent; disappeared under toxins; recurrence one year later with metastasis in brain.*

A. C., Female, 21 years of age. A rapidly growing sarcoma of the palm of the hand had been held in check for a year and a half by injections of the mixed toxins given at intervals during this period.

In June, 1894, the treatment was pushed for three weeks, at the end of which time the necrosed tumor-tissue was removed under ether. No further treatment was given and the patient regained twenty pounds of lost weight. She remained well until August, 1895, when she had a local recurrence, and amputation of the forearm was performed by Dr. SAMUEL LLOYD. Soon after there were signs of recurrence in the brain.

CASE 53. — *Small round-celled sarcoma of breast, four times recurrent; toxins three months, patient well seven and a half years.*

Miss K., aged 22 years, had been operated upon four times by Dr. FREDERICK KAMMERER of New York, for a rapidly recurrent sarcoma of the right breast. The case was regarded as hopeless from a surgical standpoint, both by Dr. KAMMERER and Dr. WM. T. BULL, who saw the case in consultation, and the toxins were advised. The injections were begun by myself and later continued by Dr. WOOLEY, of Long Branch.

Shortly after beginning the treatment, I removed two small masses from the pectoral region. After three months' treatment, there was again evidence of a local recurrence, but it has not taken place so promptly as the recurrences before the toxins had been used. It was thought wise to make another attempt at removal, which was done by Dr. KAMMERER. No further recurrence took place and the patient has remained in good health up to the present time, seven and a half years later.

Here, I believe, it is fair to assume, that the malignancy of the tumor was very much lessened by the long period of toxin treatment; though, of course, this cannot be stated positively. Microscopical examination was made after several operations, by Dr. LIBMAN of Mt. Sinai Hospital, and the disease pronounced small round-celled and polyhydal-celled sarcoma.

CASE 54. — *Recurrent angiosarcoma of breast. Almost complete disappearance; well and free from recurrence eight years later, when she died of an injury.*

Mrs. A. C., 59 years of age. Seventeen years ago received an injury to the left breast; three months later there appeared a small lump at

thé site of the blow; this grew slowly, was accompanied by some pain, and at the end of three years had reached the size of a fist. The first operation was then performed (fourteen years ago) at St. Francis's Hospital. The breast was not removed, and there were no enlarged glands in the axilla. She remained free from recurrence for seven years, when the tumor recurred; grew slowly for two years, and was then operated upon a second time at the same hospital, by Dr. GEORGE F. SHRADY, editor of *Medical Record* (May, 1889); the tumor at this time was the size of an egg, and the diagnosis made by Dr. SHRADY was sarcoma. She again remained free from disease for two years, when there was a recurrence « in situ ». She was referred to me in January, 1895, by Dr. SHRADY, as an inoperable case for toxin treatment. Examination by myself on January 20, 1895, showed a large tumor occupying the region of the left breast extending from the anterior axillary line to the sternum, and from just below the clavicle nearly to the free border of the ribs. The tumor was fairly well fixed to the chest-wall, and was markedly protuberant, made up of more or less distinct nodules, the surface of which was purple in color, and in places there was considerable ulceration with foul discharge. The tumor was unquestionably inoperable. The patient's general condition was so extremely weak that she was scarcely able to walk alone. She was admitted to the New York Cancer Hospital on January 20, 1895, and placed in the « incurable » ward. The disease was so far advanced and the general condition was so bad that no attempt was made at first to give her the toxins. After the ulcerated surface had become somewhat less foul under careful treatment, and her general condition a little improved, she was placed under treatment with injections of the antitoxin-serum of erysipelas and bacillus prodigiousus.

Effect of the injections. — In small doses of 5 to 10 minims very little effect was noticed. Larger doses, 15 to 20 minims, frequently caused intense muscular pain and an urticaria-like condition of the skin, sometimes extending over the whole back and chest, being the cause of intense itching and discomfort. Patient also complained of severe headaches, lasting sometimes for several days. The dose was never carried beyond 20 minims, but was, as a rule, given daily. This serum was prepared by Dr. Buxton in a manner similar to the

diphtheria-serum, the toxins of erysipelas and prodigosus having been injected daily into a horse for about six weeks, and the serum then withdrawn. The tumor began slowly to decrease in size, and became much more movable; the general condition of the patient likewise slowly improved. In addition to the use of the erysipelas prodigosos rerum, the mixed toxins were also given for several weeks. Treatment was continued, with occasional intervals, until September, 1895.

At this time the tumor had become so small that it could be easily removed by operation, and not having shown any great diminution in size during the past month, it was deemed advisable to remove it. Under ether the mass was removed. The periosteum of the ribs was not involved, but as the skin over the tumor was diseased a large area, 4 by 6 inches, was left to heal by granulation. No further treatment was given; the ulcer healed over as rapidly as could be expected and on December 14th it had entirely healed. There were a few small glands, about $\frac{1}{4}$ of 1 inch in diameter, in the left axilla, but, as the glands on the opposite side were even more enlarged, no attempt was made to remove them. Patient was discharged from hospital in the latter part of December 1895. Examination January 30, 1896, showed the patient in good general condition, with no evidence of a recurrence.

Microscopical examination by Prof. T. M. PRUDDEN, professor of pathology of the College of Physicans and Surgeons of New York :

I have examined a large number of sections from different parts of the tumor of breast, and, although there is considerable diversity in detail of the said growth in different parts, I think that the structures are all referable to the type of angiosarcoma which accordingly is the anatomical diagnosis.

The patient was lost sight of temporarily, but eight years afterward my associate, Dr. WM. A. DOWNES, was called to see her for a severe injury received by falling down-stairs. At this time there was no sign of the former trouble, but she died from the injuries received (fractured femur).

CASE 55. — *Large inoperable sarcoma of the abdominal wall; entire disappearance; no recurrence. Well nineteen years and ten months later.*

E. G. L., female; 28 years of age. An exploratory laparotomy had been performed at the Massachusetts General Hospital, by Dr. MAURICE H. RICHARDSON, in August, 1893. The growth was found too extensive to permit of removal, and the wound was closed. A portion of the tumor was removed and examined by the pathologist to the hospital, Prof. W. F. WAITNEY of the Harvard Medical School. The diagnosis was « fibre-sarcoma ».

The patient was sent to me by Dr. RICHARDSON in October, 1893, for treatment with the toxins. Local injections of the mixed filtered toxins were given for six weeks; then, after an interval of one month, a second course was given for four weeks. At the end of this time only a slight induration remained at the site of the tumor; this, too disappeared within a few weeks.

In the discussion of my paper including the above case, read before the American Surgical Association, in June, 1894, Dr. RICHARDSON, said :

In this case there was no doubt, according to accepted methods of diagnosis, that the woman had a malignant and necessarily fatal disease. The mass filled the right lower quadrant of the abdomen when I operated. I first incised in the median line and came down on the tumor. I then made an incision in the region, with the same result. There was nothing to be done surgically. I took out a section and had it examined. It was pronounced sarcoma. The patient was sent to New York in October. When she came back there was a little induration about the scar. In May there was not the slightest sign that could be detected. Unless the history, gross appearance, and microscopic examination were entirely wrong, this was a case which must have died sooner or later.

Report of Dr. W. F. WHITNEY, Pathologist to the Massachusetts General Hospital and Curator of the Warren Museum, Harvard Medical School :

August, 31, 1893.

The specimen from the tumor of the abdominal wall was a small, dense, ill-defined, whitish, fibrous looking mass, which on microscopic

examination was found to be made up of large numbers of small cells with a tendency to form fibres. This latter condition was more marked in some places than others. The diagnosis is fibrosarcoma.

(In a personal letter Dr. WHITNEY states that there was not the slightest doubt of the diagnosis in this case.)

Subsequent history. — The patient remained perfectly well until four years ago when she developed a fibroid tumor of the uterus, which I removed by abdominal hysterectomy. The abdominal wall at that time was found perfectly normal and there has been no trace of a return of the original sarcoma. The patient was shown before the Clinical Congress of Surgeons of North America November 12, 1912, in good health, nineteen years after disappearance of the tumor and she is still well, 19 years and 10 months, December 1913, more than twenty years later.

CASE 56. — *Round-celled sarcoma of the parotid. Patient free from recurrence six years after disappearance of the tumor under eight months treatment with the mixed toxins.*

E. S., male, 55 years old. In the fall of 1899, patient noticed a lump in the right parotid region, which increased rapidly in size until it was about as large as hen's egg, when it was operated upon by Dr WILLIAM T. BULL, on April 5, 1900. Pathological examination of the specimen by Dr. M. P. DENTON showed it to be a small round-celled sarcoma. This opinion was verified by Dr. WILLIAM H. WELCH at the Professor of Pathology John Hopkins Medical School. Shortly after, a local recurrence was noticed which increased steadily in size until October, 1900, when it was decided by Dr. BULL that further operation would be inadvisable, and the patient was referred to me for the mixed toxin treatment. The injections were begun on October 5, 1900, and continued daily for one month, doses ranging from one to two minims, which caused a temperature reaction of 99° to 102°. At the end of one month the improvement was so slight that the propriety or continuing the treatment seemed questionable. However, it was decided to give the patient a further trial and the injections were kept up from four to five times a week during the entire winter. At the end of three

months there was marked improvement. On April 1, 1901, the tumor was about one-fourth of its original size. The treatment was continued until June with gradually diminishing frequency. By this time the tumor had entirely disappeared. The patient had remained in good health up to February, 1907, when he had a severe attack of Herpes become of four following driving in a cold wind. The Gasserian Ganglion involved resulting in death. There had been no recurrence of the tumor, more than 6 years after treatment.

CASE 57. — *Large inoperable sarcoma of the abdominal wall and pelvis ; entire disappearance of tumor ; no recurrence twenty-one years after.*

J. F., male, 16 years of age. Case pronounced inoperable by Dr. L. BOLTON BANGS, at that time professor of genito-urinary surgery at the Post-Graduate Medical School-Hospital. A section of the growth was removed and pronounced spindle-celled sarcoma by Dr. H. T. BROOKS, Professor of Pathology to the Post-Graduate Medical School and the pathologist to the hospital. Dr. BANGS, referred the patient to me for treatment with the toxins, and he was admitted to the New-York Cancer Hospital in January, 1893. He was treated for nearly four months with the mixed filtered toxins of erysipelas and bacillus prodigiosus. At the end of this time the tumor had nearly disappeared, and the little that remained gradually disappeared by absorption after the injections were discontinued. There was no breakingdown. The original growth was 7×5 inches in extent, involved apparently the entire thickness of the abdominal wall, was attached to the pelvis, and from symptoms and position evidently involved the bladder-wall. The boy's general condition improved with the disappearance of the tumor.

Subsequent history. — Six years after the growth had disappeared, the patient developed a primary lesion of syphilis which ran the usual course and was finally cured by mixed treatment. This is important as showing that the original tumor could not have been syphilitic. (This case of course, was observed before the days of the Wassérman reaction.) The patient has remained in good health up to the present time and is now perfectly well and free from any recurrence, over twenty years since treatment. He was shown before

the New-York Surgical Society on numerous occasions, the last time two years ago. He was shown before its Congress of Clinical Surgeons of North-America, November, 1911, and examined by unpersonally, December, 1913.

CASE 58. — *Inoperable spindle-celled sarcoma of the pectoral region and breast; disappearance under seventy-eight injections of the mixed toxins. Patient in good health at present 18 1/2 years later.*

E. F., female, aged 42 years. Father's mother died of cancer of the breast. Patient first noticed a lump in the left pectoral and axillary region in October, 1895. This grew rapidly until it reached

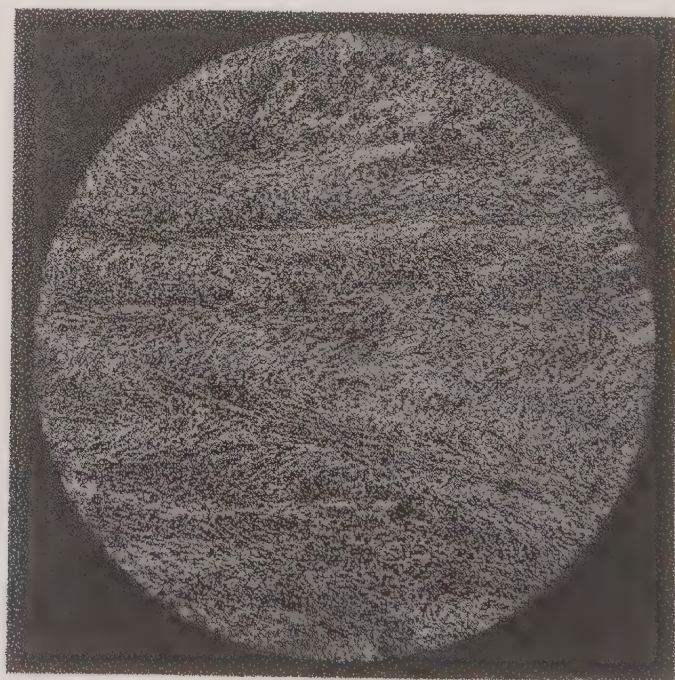


Fig. 8 (Case 58).

the size of an orange; it was firmly adherent to the deep parts and extended well into the axilla. On December 15, 1895, the patient was admitted to the Hartford's Hospital, and after consultation between Drs. STOKES and MCKNIGHT, and others, her condition was

pronounced quite inoperable. A portion of the tumor was removed under cocaine. Microscopic examination showed it to be spindle-celled sarcoma. I obtained sections of this tumor from Dr. STORRS, and the diagnosis was confirmed by Dr. E. K. DUNHAM and Dr. B. H. BUXTEN, of New York, and, finally, by Professor W. H. WELCH, of John's Hopkins Medical School. The patient's general health had become poor, and she had lost twenty-four pounds in weight. The treatment with the mixed toxins was immediately begun by Drs. R. H. GRISWOLD and STORRS under my direction. Almost immediately after the beginning of the treatment, the tumor began to decrease in size, and in a little more than one month's time, she had regained her normal weight of 154 pounds. After she had seventy-eight injections, the tumor entirely disappeared and she received no further treatment. The patient has remained perfectly well up to the present time. I showed her in good health with no trace of tumor before the Congress of Clinical Surgeons of North America, November 12, 1912. She is at present in good health; last report December 2, 1913, eighteen years after treatment.

Case 59. — *Large, recurrent spindle-celled sarcoma of cheek.*

Entire disappearance; patient well six years later.

F. Q., male, 63 years of age. In January, 1904, noticed a swelling in the middle of the right cheek; this was removed one week later, but recurred within a few weeks and grew very rapidly. On March 2, 1904, the patient was referred to me. At this time there was a hard mass in the central portion of the right cheek, 2 inches in diameter and $\frac{1}{2}$ inch in thickness.

An attempt to remove the growth was made, but this was impossible without sacrificing almost the entire cheek. Microscopical examination made by Professor E. K. DUNHAM showed the growth to be a spindle-celled sarcoma. Immediately after the wound had closed, the patient was put upon the combined X-ray and mixed toxin treatment which was continued for about three months, at the end of which time the growth had disappeared and the cheek had resumed a normal appearance. The patient was examined by me and found to be well six years later.

CASE 60. — *Mixed-celled sarcoma of the parotid, three times recurrent, treated with injections of the mixed toxins for six months; patient perfectly well ten years later.*

Mrs. B., aged 25 years; previously operated upon three times by Dr. WILLIAM T. BULL for mixed-celled sarcoma of the parotid. The microscopical examinations in this case were made by Dr. FERCUSSON, pathologist of New York Hospital, and Drs. B. H. BUXTON, and E. K. DUNHAM, of the General Memorial Hospital. She was referred to me by D. BULL in 1897 for the toxin treatment, and there was no hope of benefit by further operation. At this time the tumor was about the size of a small egg, infiltrating the entire parotid gland on the right side; cervical glands not enlarged. The mixed toxins were given in small doses two to three times a week, with occasional intervals for four months. The tumor slowly decreased in size until there was very small, freely movable nodule left, which was excised under examination, showing no longer any traces of sarcoma. The patient was in perfect health in January, 1907, ten years later, since which time I have been unable to trace her

CASE 61. — *Round-celled sarcoma of the lip, three times recurrent, entire disappearance under four week's treatment with the mixed toxins. Patient has remained in good health up to the present time, sixteen years later.*

M. S., female, aged 3 years, daughter of a physician, in Tacoma, Washington. Patient first noticed a small spot, resembling a mosquito bite, on the right side of the lower lip, in September, 1896. It grew rapidly and about four weeks later it was removed by Dr. JAMES R. YOCOM of Tacoma, Washington. It was not regarded as malignant at that time, but the specimen was kept in alcohol. In October the growth began to reappear. Examination was then made of the specimen previously removed, and it was found to be round-celled sarcoma. A much more extensive operation was immediately done, the entire thickness of the lip being removed, going widely beyond the scar and tumor. The tumor at that time was about the size of a pea and markedly indurated. A few weeks later it again occurred in the region of the scar. Feeling that further

operation would be of little avail, the child was sent to me for treatment with the toxins. The tumor at that time involved the entire scar and extended from the mucous membrane of the lip, downward about one and one-half inches, and was increasing rapidly in size. The mixed toxins were begun February 10, 1897, and injected into the tissues of the lip near the tumor and repeated in doses just sufficient to give her a slight reaction, but only once producing a chill. The filtered toxins were given except in two instances. The tumor tissue very soon lost its vascularity, began to shrink and to lose the glossy tense appearance. After four weeks' treatment, there was apparently very little of the tumor tissue remaining, but with a view of decreasing the chances of relapse, by removing any possible sarcomatous tissue that might be present, I decided to excise the entire scar tissue resulting from the previous operation. This was done by making the usual incision adopted in epithelioma of the lip, cutting about one-fourth inch beyond the scar tissue. The tissue removed was carefully examined microscopically by Dr. B. H. Buxton, assistant pathologist to the New York Cancer Hospital, and no sarcomatous elements could be found in any portion of the tissue removed. The injections of the filtered toxins into the arm were used with intervals of rest for a year afterward. The patient is still free from recurrence, sixteen years after. She has since graduated at Welleslev College and examined her carefully two years ago.

CASE 62. — *Inoperable round-celled sarcoma of the chest wall, involving ribs. Disappearance under toxins and X-rays. Recurrence and death later.*

G. C., aged 16 years; enjoyed good health up to 1903, when he had an attack of what was considered to be pleurisy with effusion. He was aspirated, but the dulness over the chest persisted, and he rapidly lost flesh and strength. He was sent south, without improvement, and in October, 1903, entered the Johns Hopkins Hospital, where he was operated upon for a supposed empyema. A large incision was made, revealing a necrosis of the eighth and ninth ribs, and behind these some gelatinous masses were found. These were partially removed and examined by Dr. WELCH, who pronounced them round-celled sarcoma. The patient was referred to me, and on May 26, 1904,

was admitted to the General Memorial Hospital, where for two months the toxins were regularly administered; in addition, he received X-ray treatment three times a week. At that time patient was so weak that he could hardly walk. There was a mass about the size of a man's hand over the ribs, with an extensive sloughing area in the centre. The improvement was very rapid, and when he left the hospital in the fall of 1904 there was no trace of the tumor left; the patient had gained 25 pounds in weight and seemed in perfect health. He returned to his home in Canada, where his family physician had been instructed to continue the toxin treatment in smaller doses two to three times a week.

By the end of January, 1905, the patient returned to New-York for examination, and there was evidence of a local recurrence, which at first again showed some improvement under toxin treatment, after a few weeks, however, the tumor began to slowly increase in size in spite of large doses of the toxins and regulated prolonged X-ray treatment. The patient gradually failed and died in October, 1905.

CASE 63. — *Recurrent, inoperable spindle-celled sarcoma of the parotid. Entire disappearance under the mixed toxin treatment; perfectly well six years; then died of other trouble.*

W. L., 41 years of age; maternal aunt died of cancer of the breast. In September 1896 the patient received a slight injury to the left parotid region. In the early part of 1897 a swelling was noticed which increased in size and was removed by Dr. J. W. WRIGHT of Bridgeport, Conn., in March, 1897. The submaxillary glands were found to be involved in the disease. The tumor recurred and two further operations were done in April, 1897, it was then found too extensive to permit of removal and the case was considered completely hopeless. Microscopical examination showed the tumor to be spindle celled sarcoma. The mixed toxins had been tried for three weeks in Bridgeport, without any apparent improvement. The patient was admitted to my service at the Post-Graduate Hospital in the early part of August, 1897. Physical examination at this time showed a large tumor occupying the whole left parotid region, markedly protuberant. The submaxillary and nearly all the cervical glands on the left side were

extensively involved. The general condition of the patient was excellent and the toxins were pushed very vigorously, the injections being given daily, both locally and systemically. At the end of a week there was very marked improvement, as shown by diminished vascularity and decrease in the size of the tumor. At the end of ten weeks the growth had entirely disappeared. The patient returned home and no treatment was thereafter given. He remained perfectly well, without any trace of a recurrence for six years when he suddenly died of gastric hemorrhage from an ulcer.

CASE 64. — Spindle-celled sarcoma of the abdominal wall. Entire disappearance following thirty injections of the toxins. Patient well one and one-half years later when she was lost sight of.

M. S., female, aged 18 years, was admitted to the New York Cancer Hospital December 29, 1896, with a tumor in the lower portion of the lower portion of the abdomen of several months' duration. Exploratory laparotomy was performed by Dr. JOSEPH BRETTACER, assisted by Dr. GEORGE W. JARMON, the attending gynecologist. A large mass was found in the abdominal wall, both intra- and extra-peritoneally but it had no connection with any of the abdominal organs. It was regarded as inoperable and a portion was removed for examination and pronounced by the hospital pathologists, Drs. E. K. DUNHAM, Professeur Pathology Bellevue Medical College and B. H. BUXTON, as a spindle-celled sarcoma. The case was transferred to my service in order to have the toxin treatment tried. The first injection was made January 19, 1897. The toxins used were prepared by Dr. BUXTON from cultures of streptococcus that had been passed through fifty-five rabbits, thus attaining a very high degree of virulence. After thirty injections, the largest dose being six minims of the filtered toxins, the tumor had entirely disappeared. Very little pain and discomfort resulted from the treatment, and but four chills occurred the entire time. This case was shown in April, 1897, before the New York Surgical Society. The patient went to Europe one and one-half years after the treatment was started, when she was still well; she could not be traced later.

CASE 65. — *Very large fibro-sarcoma of gluteal region and thigh, recurrent, Inoperable, gradual disappearance under the toxin treatment patient well nineteen years later.*

Mrs. S., 30 years of age, referred to me by Dr. HARMON, of Hartford, Conn. The patient was admitted to my service at the New York Post-Graduate Hospital in October 1893. Two years previously a very large primary tumor had been removed by Dr. CHAS. McBURNEY, at Roosevelt Hospital and pronounced fibro-sarcoma; it recurred and the proved beyond operation the case was regarded as hopeless by Dr. Mc. BURNEY. Physical examination at the time the treatment was begun, showed a very large tumor occupying the left gluteal region, and involving the muscles and fascia of the upper of the thigh posteriorly. The tumor was so extensive that any attempt at removing it by operation was out of question. The mixed toxins were immediately begun, the injections being made locally and the dose gradually increased up to the point of getting a marked reaction. The improvement was very slow. At the end of three months' continued treatment he left the hospital, and while there was considerable decrease in size, there still remained a large tumor. This continued to decrease in size without any further treatment. Examination five years later showed two small hard movable masses at the site of the original tumor. These were excised, chiefly in order to determine the histological structure. Microscopical examination showed them to be only fibrous tissue, all the cellular elements having been absorbed. The patient has remained in good health up to the present time, twenty years later. She was shown before the Clinical Congress of Surgeons of North America in November, 1912. And is still well over 20 years after treatment; my last examination of patient was made December 1913.

CASE 66. — *Round celled sarcoma of the back lumbar and sacral region with metastasis in the lower jaw; disappearance under two and one-half months' treatment with the mixed toxins.*

C. E. C., male, 27 years old, always in good health, with family history good, and no history of injury. The patient first noticed a tumor in the lower lumbar region in September, 1907; it grew with

great rapidity and was operated upon in the latter part of September by Dr. J. C. BIDDLE, of Fountain Springs, Pa. The tumor than was the size of two fists. The pathological examination of the growth was made by Dr. JOHN FUNKE, Pathologist of the Jefferson Medical College Hospital, who pronounced it to be a large roundcelled sarcoma.

On November 19, 1907, the patient was admitted to the General Memorial Hospital. Examination showed an unhealed wound in the lumbar and gluteal region, 6×8 inches in area, the unhealed portion being the shape of an excavation about 1 inch lower than the surface of the surrounding tissue. The lower jaw showed a tumor beginning about 1 inch to the left of the symphysis, extending to the left nearly to the angle of the jaw, the growth seemingly occupying the entire thickness of the jaw. The patient was put upon the mixed toxins at once, $\frac{1}{4}$ minim being the initial dose given in the gluteal region. This was gradually increased until a temperature of 102-103° was obtained. Under these systemic injections the tumor of the jaw slowly became smaller and much softer. As it became fluctuating, I made an incision over the most protuberant part and found a highly vascular tumor extending down to the periosteum. The patient's general condition slowly began to improve under the treatment. In November, 1908, I showed him before the Orthopedic Section of the Academy of Medicine, at which time he had gained sixteen pounds in weight, and there was no longer any evidence of a tumor either in the jaw or the lumbar region. The wound had entirely healed. He had had altogether 49 injections of the toxins, beginning with $\frac{1}{4}$ minim, and increasing up to 8 minims. All but five injections were systemic into the buttocks.

Patient states in a letter, dated March 24, 1911, that he is still in perfect health, and his weight has been maintained at 206 lbs. without variation a year or more. I showed before the Congress of clinical surgeons of North America, November 12, 1912, and he is still well at present February 1914, six and a half years after treatment.

Novembre, 1907.

Pathological report. — Specimen consists of a globular mass measuring 1 by 1.5 by 2 centimetres; weight 2 grams.

It is neither hard nor soft; it is grayish-white in color and cuts with ease; the incised surfaces are granular and greyish-white.

The specimen was received in alcohol, fixed in Heidenhain's solution and embedded in paraffin. Sections were cut and stained with hematoxylin and by Van Gieson's method.

Histology. — The sections vary in their architecture. In some places, usually at the periphery they are composed for the most part of fibrous tissue which is rather loosely woven. Occasionally the strands are dense, sometimes very delicate. These dense and delicate fibrils anastomose forming a meshwork. The meshes vary greatly in size and shape, and contain a translucent substance and several types of cells. Some of the elements are clearly polymorphonuclear leucocytes; they are very abundant and still others spindle. Some of these stain very poorly. The nuclei are round or oval, have a reticulated structure in which are fine granules and very little chromatin. The protoplasm of the round and oval cells is vacolated and granular, that of the spindle-shaped cells is less granular and takes the acid dyes fairly well. Among the fibrous tissue are numerous bloodvessels of varying sizes. Some are empty others are occupied with blood; some have thin, others thick walls.

The central portions of the sections are less dense and largely cellular. Few fibrous strands traverse these areas and anastomose forming large meshes which act as a vessels. The cells vary in shape and size. Some are round others oval or polyhedral; they measure from 15 to 40 in diameter. The nuclei are round or oval and many have nucleoli; they stain poorly with the basic dyes. Some cells contain more than one nucleus, as many as five have been found in one cell. The protoplasm is granular, abundant, stains poorly with acid stains and is not infrequently vacuolated. The vacuoles in all probability were occupied during life by some soluble substance. The cells rest upon the fibrous tissue from which they probably originated.

Diagnosis and remarks. — The denser portions of the sections bear a striking resemblance to the structure seen in Hodgkin's Disease, although the eosinophile cells are not found. The more rarified portion is undoubtedly malignant, being large round-celled sarcoma.

Respectfully submitted,

(Signed) JOHN FUNKE.

Res. Pathologist, Jefferson Medical College Hospital.

CASE 67. — *Recurrent Round-Cellled sarcoma of the uterus, Inoperable. Entire Disappearance under toxin treatment. Patient well five-and-three-quarters years.*

Mrs. McM., 50 years of age; referred to me by Dr. HOWE, of Hartford, Conn. in April 1908. Had been operated upon at the Hartford-Hospital, a year before for a large tumor, pronounced by Dr. STEINER, the pathologist to the hospital, a round-celled sarcoma. The tumor recurred and the patient was sent to me as a totally inoperable case. Examination at this time showed the whole pelvis filled with an infiltrating tumor which was so hard that, clinically, it resembled carcinoma, rather than sarcoma. Her general health had markedly failed and bladder symptoms had developed. I gave a very bad prognosis and told Dr. HOWE that all that could be expected was to hold the disease temporarily in check. The toxins were begun on April 7th and continued for four weeks by Dr. HOWE. The patient's general health soon began to improve and the tumor steadily diminished in size until August, when the treatment was stopped for two weeks. Immediately the severe pains returned and Dr. HOWE resumed the toxins, giving the injections every other day through September; then twice a week, then once a week, and finally, once in ten days. In a letter from the patient, dated December 14, 1908, she states, « I am so well that I can hardly believe that I am myself; I cannot remember ever being so well, etc. The treatment was continued over a period of two-and-a-quarter years, and she received 118 injections in all. I showed the patient before the Clinical Congress of Surgeons of North America, November 12, 1912, and have recently heard that he is still well more than six years of the treatment.

CASE 68. — *Malignant leiomyoma of the uterus, Recurrence. Disappearance under the toxin treatment. Patient well at the present time, more than six years since the beginning of the treatment.*

Miss X., age 42 years, single; referred by Dr. LEONARD WHEELER, of Worcester, Mass., on September 26, 1907. Mother died of malignant tumor of the uterus, without operation. In February 1907, the patient has been operated upon at the Boston City Hospital for a tumor of the uterus which was clinically thought to be a fibroid,

Microscopical examination made by Dr. MALLORY, professor of pathologist of the Harvard Medical School, showed it to be leiomyoma. During the summer, the patient began to have intermittent attacks of frequent micturition, accompanied by pain. Vaginal examination, made by Dr. EDWARD REYNOLDS, of Boston, September 1907, revealed a mass which had almost doubled in size since the last examination a few weeks before. Dr. REYNOLDS considered the growth malignant and inoperable and referred the patient to me for the toxin treatment.

Physical examination by myself, September 26, 1907, showed an infiltrating tumor occupying the whole lower portion of the pelvis, apparently involving the bladder wall. The tumor was hard in consistence, irregular in outline, and had the « feel » of carcinoma rather than sarcoma. That it was a malignant tumor of some type was fairly certain from its recurrence, its infiltrating neighboring tissues and its rapid growth. It was entirely inoperable.

The patient was suffering a great deal of pain, had frequent and painful micturition, and had lost considerably in general health. Although a bad prognosis was given, I thought it worth while letting her have a brief trial with the toxins. She was admitted to the General Memorial Hospital where she remained one month. The treatment was given five times a week in doses from one-half to four minims. At the end of this time there was marked cessation of the pain, and the tumor had become somewhat softer and less fixed. The patient was then sent home where the treatment has been continued by her family physician, Dr. LEONARD WHEELER three to four times a week, with occasional intervals of two to three weeks of rest, for three years. In the summer following the beginning of the treatment, during the hot period, the toxins were left off for nearly two months. During this time her former symptoms returned and the growth seemed to have increased somewhat in size. The injections were resumed and, with continued treatment, the symptoms again entirely disappeared, and the growth became smaller and softer. The toxins were discontinued entirely in January, 1910, after having been continued for a period of nearly three years. Her general condition has been perfect practically the whole time. At present six later years, she weighs more than she ever did in her life, and is in splendid health; local examination shows little more scar tissue than is natural to a hysterectomy. I showed her before the Clinical Surgeons of North-

America, November, 12, 1912, my last examination made December 3, 1913, Showed the patient in the best of health over six years afterwards.

CASE 69. — *Fibrosarcoma of anterior crural new sheaths, involving pectineal muscle and glands of groin, treated with the mixed toxins after operation; patient well at present, three years later.*

B. C. C., male, 7 years old. Family history : grand-mother died of cancer of breast. Patient was struck in the groin by a base-ball in November 1910. Mother who always bathed him,

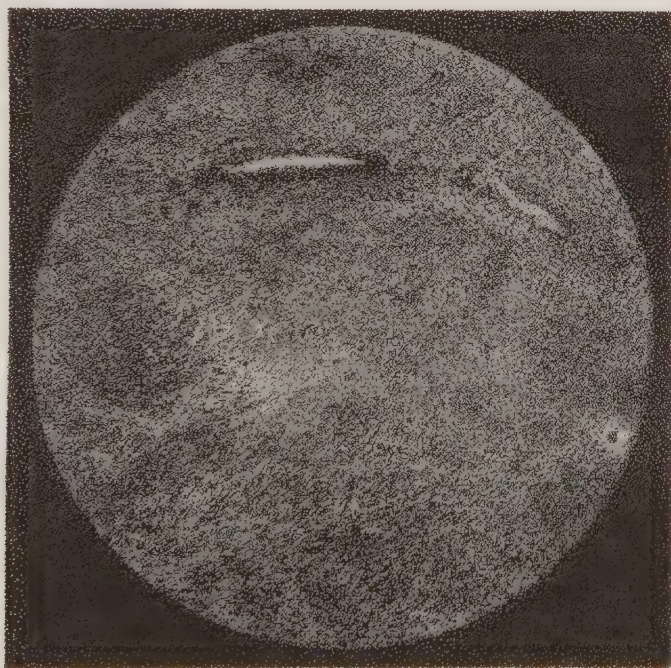


Fig. 9 (Case 69).

noticed nothing unusual; three days later, however, the boy developed a slight limp on the right side; on examination a small lump was found in the right groin, just below Poupart's ligament; this doubled in size in three days. He was taken to Dr. BAER on December 4th and an operation was performed on the 10th.

On December 29, 1910, Dr. WALTER FISHER of Baltimore, referred the case to me in regard to the advisability of treating him with the toxins for an apparent recurrence which had developed at the site of the previous operation.

Physical examination at this time showed a recent cicatrix 3 ins. long, in the right groin; a small mass could be felt in the inguinal region which I believed to be a recurrence. The toxins were immediately begun in small doses and gradually pushed to the point of giving a moderate reaction. After three weeks he was sent home and the injections were continued by Dr. FISHER.

The patient proved very susceptible and could not take over 2 minims. He gained weight steadily under the treatment which was continued for three months. I examined him from time to time and he was also examined by Dr. BLOODGOOD and Dr. FISHER. The microscopical examination at the Johns Hopkins laboratory « was fibromyxosarcoma of the nerve sheaths, particularly of the anterior crural nerve ». The glands also showed sarcomatous involvement. A letter received from the patient's mother, dated July 7, 1913 states : « I am glad to report that Beverley continues in very good health. » He is still well January 1914, more than three years later.

CASE 70. — *Sarcoma of the pelvis, Recurrent after Hysterectomy, entirely inoperable patient well at present, eighteen years later.*

M. L., female, 35 years of age, operated upon at the Post-Graduate Hospital in 1894, by Dr. STANNERT, a hysterectomy being done. The pathologic specimen was lost during the removal from the old to the new building (was pronounced Sarcoma). The disease recurred shortly afterward and Dr. STANNERT did an exploratory laparotomy. He found a large tumor which was quite inoperable. The patient was then referred to me for the toxin treatment. The injections were given for several months at the New York Cancer Hospital, in 1895. Under the treatment the tumor diminished so much in size that another attempt was made to remove it. A very large vascular tumor was found, occupying the larger part of the pelvis, and so adherent, that it was regarded as inoperable. The patient left the Hospital shortly afterward and all trace of her was lost until the early part of 1908, when she came to my service at the General Memorial Hospital for a

ventral hernia, following one of the laparotomy incisions. She stated that after leaving the hospital in 1894 she returned to her home in Ireland where she remained for eight years. The tumor had gradually disappeared after she left the hospital and she had been in good general health up to 1907. My associate, Dr. W. A. DEWNEs operated upon her for the ventral hernia and careful examination of addominal cavity showed no trace of a tumor either in the abdomen or pelvis. The patient was still well in November 1913, 19 years afterwards.

CASE 71. — *Inoperable spindle-celled sarcoma of the uterus, rendered operable under six months' toxin treatment. Patient in good health at present? Two and a half years later*

Mrs. F. S., 42 years of age, had noticed a rather rapidly increasing tumor in the abdomen in the latter part of the year 1910. This was operated upon by Dr. L. R. G. CRANDON, of Boston, in April 1911. Dr. C. found a tumor involving the uterus which was so large and associated with such extensive adhesions that he believed it to be entirely inoperable. A specimen was removed and sent to the Harvard laboratory for microscopical examination, and Dr. F. B. MALLORY's report reads as follows :

Microscopic section shows a cellular spindle-celled growth. No mitotic figures can be found. A provisional diagnosis of fibro-sarcoma or leiomyoma was made. On going over the section again, I am almost convinced that it is a fairly cellular, somewhat edematous leiomyoma.

Shortly after recovery from the operation, the patient was referred to me with regard to the advisability of the toxin treatment. I believed the toxins indicated in this case and began the treatment with injections made into the gluteal region, May, 1, 1911, gradually increasing the dose up to the point of getting a marked reaction. The treatment was administered four times a week. At the end of four weeks there was a slight decrease in the circumference of the abdomen. The treatment was then continued by her family physician in Boston. At the end of six months' treatment, the circumference of the abdomen had diminished four inches. There was no decrease in weight.

There was also marked increase in mobility of the tumor which,

together with the decrease in size, furnished strong clinical evidence that the growth was a sarcoma and had been favorably affected by the toxins. In January, 1912, the condition had become sufficiently favorable to warrant another attempt to remove the tumor by operation. The patient was admitted to the General Memorial Hospital in January, 1912, and operated upon by my self, with the assistance of my associate, Dr. Downes. On opening the abdomen, a tumor was

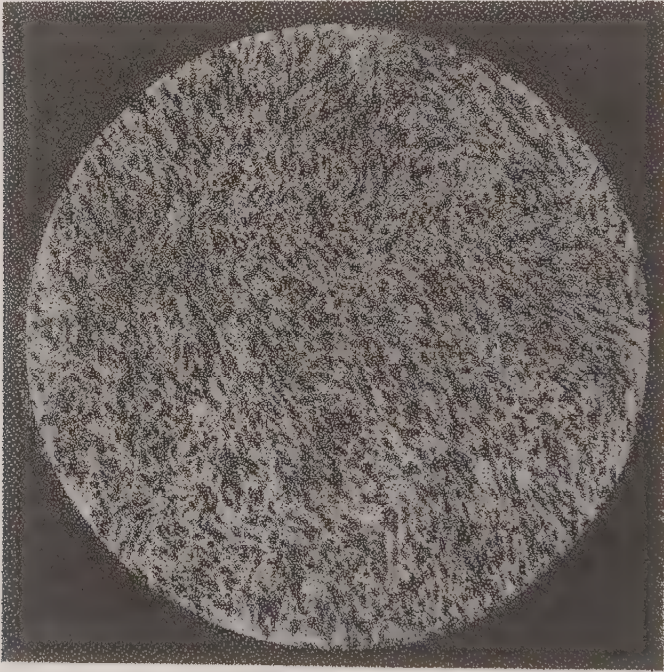


Fig. 10 (Case 71).

found largely filling up the abdominal cavity and extending nearly to the diaphragm. It seemed to be chiefly retro-peritoneal the lower portion was connected with the uterus. The intestines were adherent in numerous places. In some portions the covering of the tumor appeared to be almost continuous with the mesentery and the small intestine. By careful dissection it was finally freed and the whole tumor, uterus, ovaries and tubes were removed. The right ureter was exposed for a distance of 3 inches. The patient recovered from the operation and made a rather slow convalescence. She later

regained her normal health, and has been perfectly well up to the present time, two years since the operation, or two and one half years since the beginning of the treatment. Careful examination two weeks ago failed to reveal any trace of a return. The tumor was examined by Dr. W. C. CLARK, pathologist of the General Memorial Hospital, and pronounced « spindle-celled sarcoma ».

CASE 72. — *Recurrent inoperable spindle-celled sarcoma of the ovary. Disappearance under toxin treatment. Recurrence later: Ending in death.*

M. C., 16 years. Patient fell down-stairs, injuring her abdomen in 1908. About six months later noticed pain and swelling in the lower portion of the abdomen, and in November, 1909, the first operation was performed by Dr. BLASUCCI of New York City, who found a large tumor involving the left ovary, for which he performed ovariectomy. Microscopical examination proved it to be round- and spindle-celled sarcoma. Recurred quickly followed and a second operation was performed by Dr. HERBERT T. MERRIS, and Dr. BLASUCCI at the Murray Hill Sanitarium, on February 28, 1911. Dr. MERRIS stated that a large retroperitoneal tumor was found filling up the pelvis and lower part of the abdomen. It was entirely inoperable and hence the wound was closed. The patient's general condition at this time was bad; she had lost much weight and was cachectic.

I saw her in consultation, on March 7, 1911, and on my advice the mixed toxins of erysipelas and bacillus prodigiosus were begun and carried out, at first by her own physician. The patient proved very susceptible to the toxins, and had severe chills from small doses (2 to 3 minims). Shortly after the treatment was begun, decrease in the size of the tumor was noticed, and on May 2, 1911, although the patient had no toxins for three week, palpation revealed no tumor whatever. She had been running an irregular temperature for two weeks, up to 102 to 103°, but this had gradually fallen to normal. Her appetite was poor and she was slightly anaemic. The continued slight temperature was thought to be due to absorption of broken-down tumor material. The patient returned home and the treatment was continued partly by her physician and partly by her sister.

In response to an inquiry, Dr. BLASUCCI under date of January 9, 1914, writes :

She died, September 28, 1911, about twenty-two months after my operation of ovariectomy.

CASE 73. — *Spindle-celled sarcoma of abdominal wall, involving bladder.*

Mrs. H. L. G., referred to me, in April 1901, with an inoperable tumor in the supra-pubic region of about four months duration. I performed an exploratory operation removing a portion of the tumor and microscopical examination made by Dr. B. H. BUXTON, proved it to be a spindle-celled sarcoma. The entire thickness of the abdominal wall and some of the bladder wall was involved, which made it impossible to remove the tumor surgically. She was put upon the mixed toxins and the treatment was continued for three months. The tumor entirely disappeared and the patient has remained well since.

In a letter, dated July 13, 1904, she stated :

It is three years and a few months since I have taken the toxins. There seems to me no doubt of the cure effected by your treatment. My general health has improved slowly and I am stronger than I ever was.

A later letter received from the patient, dated October 17, 1913, reads :

I am thankful to say that there has been no return of the disease for which you treated me. My general health is good, and perhaps I am a little stronger.

CASE 74. — *Inoperable round-celled sarcoma of the ovary.*

Mrs. E., 26 years old, referred to me by Dr. H. C. COE, to whom she had been sent from Manila, P. I., by Dr. H. EUGENE TAFFORD, who, under date of December, 20, 1904, described the case as follows :

« Some six weeks ago, Dr. BAILEY, U. S. A., was called to treat Mrs. E. for what he at first thought was inflammation of the left ovary : this he treated for about 2 weeks when there developed a tumor. He sent her to me for operation in consultation with

major E. C. CARTER, U. S. A. Upon examination I found a mass filling the pelvis and about two inches above; the uterus was crowded down almost to the external genitals and the mass was not movable. There was considerable tenderness of the lower abdomen which did not admit of much palpation and the abdominal muscles were rigid. She was prepared for operation and upon becoming anaesthetized the abdominal muscles relaxed and the tumor was seen to have grown up to, and a little above, the umbilicus to the right side. Upon opening the abdomen, the mesentery was found adherent to the outer surface of the tumor. This being dissected free and a portion incised, the tumor was seen to be nodulated in character, of a dark bluish-white color and upon passing the and down its anterior surface to the pelvis, the greater portion was found adherent. Upon pulling the tumor forward, enormous blood vessels were seen covering the back of it and springing from and above the posterior brim of the pelvis. From the general appearance, its rapid growth and its extreme vascularity, we decided it was a malignant growth, probably sarcomatous. On endeavoring to free the tumor from the blood vessels, we found it was not adherent, but was growing apparently from the whole of the pelvic wall and its bleeding so freely convinced us that it would be wisest to abandon further interference, particularly as her husband desired her to reach home to see her parents before dying. The incision was closed and the patient was more comfortable having less temperature than was previously present. A portion of the tumor was tied off and excised and sent to the Government Laboratory. I enclose a copy of the report which convinces me that the patient will hardly live to reach you. »

Pathological Report : An apparently rapidly growing and infiltrating very cellular growth of probably perithelial origin : perithelial Haem-Angio-Sarcoma. (H. E. STAFFORD.)

Physical examination, February, 20, 1905, showed a hard tumor occupying the whole lower portion of the abdomen from the umbilicus to the Symphysis pubis apparently involving the abdominal wall as well as the deeper structures : firmly fixed : no swelling of glands of groin. Slight loss of weight : some pain.

It was decided to give the patient the benefit of a trial with the toxins, which was started on the 24th of February and continued up

to June 1st, during which time she received forty-seven injections in all. Under the treatment the tumor slowly and steadily decreased in size, and became more movable so that it was decided to try to remove the remainder of it by operation. This was done on June 12, 1903, by Dr. Cœ and my self. Operation showed a mass the size of a child's head, freely movable, small pedicle was removed rapidly and easily. The tumor was found to be round-celled sarcoma and filled with necrotic areas. Patient made an uneventful recovery, and gained 26 lbs. in six weeks. In the latter part of the year she became pregnant and was delivered of a healthy child in the summer of 1906. The patient remained free from recurrence until her death, from acute pneumonia in February, 1907.

Her family physician Dr. D. L. MOORE, wrote me, December, 1906. «There was no lighting up of the pelvic trouble, and no recurrence of the original trouble could be made out on examination.»

CASE 73. — *Recurrent sarcoma of the cheek.*

Mrs. D. L., aged 40 years, family history good. In June, 1897, patient received a blow upon the left side of her face. Swelling appeared at once, situated between the skin and mucous membrane, and then disappeared within a few days, only to return a few weeks later. The tumor grew slowly until it had reached the size of one-half hen's egg, when it was operated upon by Dr. THOMAS, of Roseland, B. C. The disease shortly recurred and at the time of the second operation it had reached the size of a goose egg. In November, 1898, another recurrence was noticed. The diagnosis of sarcoma was confirmed by microscopic examination. The patient was referred to me in March, 1899, at which time, physical examination showed a cicatrix, beginning at the angle of the mouth and extending directly backwards for a distance of $2\frac{1}{2}$ inches, and $\frac{1}{2}$ inch in width. In the center of the scar, and extending nearly to the angle of the mouth, was a tumor about $\frac{3}{4}$ inch thick and about 2×3 inches in area, firm in consistence. It was impossible for the patient to open her mouth more than three-quarters of an inch. She entered the New York Cancer Hospital and was immediately put upon the mixed toxins, the injections being made locally. The treatment was continued for six weeks, at the end of which time the tumor had entirely

disappeared. I have been unable to trace the subsequent history of the patient.

CASE 76. — *Sarcoma of the deltoid region. Recurrent.*

H. B. M., male, 56 years old, family history good. In the summer of 1902, a small tumor, which had existed for many years, began to grow rapidly, and in September, 1902, Dr. W. A. Brooks, of Boston, performed an operation removing the tumor, as well as some of the deltoid muscles. Pathological report, of J. H. Wright, Mass. General Hospital Laboratory reads: Spindle-celled sarcoma. Patient was referred to me on February 12, 1903, at which time, physical examination showed a cicatrix 4 $\frac{1}{2}$ inches long, in the upper and lower extremities of which could be felt a small mass, apparently a recurrence of the growth. The mixed toxin treatment was started at once, and continued for several months by the local physician. When last examined in 1912, nine years later, the patient was still well, with no sign of a recurrence.

CASE 77. — *Inoperable sarcoma of the iliac fossa.*

E. S., male, aged 14 years. A year and a half previously he had been dragged under a trolley car, causing contusions about the pelvis. In January, 1895, he began to feel pain in the right groin and a tumor soon developed in the right iliac fossa. Exploratory laparotomy by Dr. GEORGE B. FOWLER, of Brooklyn, on March 7, 1897, showed a vascular tumor, filling up the whole right iliac fossa extending upward 3 inches above the crest of the ilium and Poupart's ligament. The tumor was so vascular that Dr. FOWLER did not think it wise to remove a portion for examination. He closed the wound and regarded the case as entirely hopeless. The condition continued to grow rapidly worse after the operation and on April 10, 1897, the mixed toxins were given as a last resort. The treatment was carried out under my direction by Dr. G. H. DAVIS, of Brooklyn, and continued for several months. The improvement was immediate and rapid. At the time it was begun, the patient was extremely emaciated, with marked cachexia and could not have weighed more than sixty pounds. Within the next three weeks he was walking about and had gained

at least ten pounds in weight. Examination of the abdomen showed that the tumor had almost entirely disappeared. The injections were not made into the tumor, but into the gluteal region and upper thigh. A few months later he developed a fluctuating swelling over the ilium behind. The skin became broken, and a slight infection occurred, causing some temperature. I incised the swelling, evacuating several ounces of degenerated, broken down tissues. No bare bone was detected at any time. The curettings of the walls of the cavity were carefully examined and not the slightest evidence of tuberculous disease could be found, practically verifying the original diagnosis of sarcoma. Another, similar operation was performed on April 10, 1898. The toxins were continued, with occasional intervals of rest, for three years. On February 6, 1903, six years later, I again examined the boy and found no signs of a recurrence. He died two years later of pericarditis.

CASE 79. — *Spindle-celled sarcoma of the arm resulting from trauma.*

Mrs. H. W., aged 23 years; married but has no children. The patient was referred to me in March, 1912, with the following history :

Three years ago she received a cut in the wrist on the palmar surface just above the joint, from a piece of glass. The glass was removed and the wound healed quickly. One month later she noticed a hard swelling, the size of a walnut, in the middle of the biceps region of the upper arm. This slowly increased in size for two years. Dr. BERG, of the Mt. Sinai Hospital, performed the first operation in November, 1910. An incision 10 inches long was made, from the external condyle up nearly to the head of the humerus. The tumor occupied the anterior aspect of the right arm, midway between the biceps and triceps muscle; it was apparently of facial origin but had begun to involve the periostum. A piece of bone was chopped off. Microscopical Examination, was made by Dr. F. S. MANDELBAUM, Pathologist of the Mt. Sinai Hospital, who gave the following report :

The specimen consist of a sausage-shaped tumor, 12 centimetres long, 5 centimetres wide, and 4 centimetres thick. On section it appears somewhat fibrous and is composed of two types of tissue, one white and succulent, the other yellowish. In general appearance it

resembles somewhat that seen in desmoid of the abdominal wall, but there are areas of fat tissue and considerable soft tissue not seen in typical desmoids. Microscopic diagnosis : Fibro-sarcoma.

The growth quickly recurred, and the patient was referred to me, March 1, 1912, at which time there was diffuse swelling of the entire two-thirds of the arm, the circumference 3 inches above the condyle being $10 \frac{3}{4}$ inches. The tumor extended seven inches longitudinally, and apparently involved three-quarters of the circumference of the arm. Skin was of a purplish color, movable over the inner portion of the tumor, but apparently adherent at the outer portion. Clinically it had the appearance and consistence of an infiltrating spindle-celled sarcoma of the fascial region. X-rays taken at that time showed slight involvement of the periosteum only. The patient was immediately put upon the mixed toxin treatment which was continued by her family physician. The injections were given alternately into the pectoral region and tumor itself. Severe reactions followed, with an occasional temperature of 104° . There was considerable limitation of motion at the elbow, the forearm admitting only 30° of flexion.

The injections were continued very regularly by her family physician, and I had frequent opportunities of watching the case. Physical examination, February 13, 1913, one year later, showed that the treatment had not only checked the progress of the growth, but there was also diminution in circumference, the same measuring $\frac{1}{2}$ inch less than at the time of the last examination. There is slight increase in flexion, and she has gained 2 to 3 pounds in weight. X-ray photographs taken at this time, showed no further invasion of the bone. Last examination, made Decembre, 1913, shows little change since last note; general condition good. The case cannot yet be regarded as more than improved.

CASE 80. — *Melanotic round and oval-celled sarcoma of toe recurrent in groin.*

Dr. E. B. D. In the spring of 1906, patient first noticed a Naevus on the left second toe. This became ulcerated and painful. Two years later the toe was amputated and microscopical examination

showed the growth to be melano-sarcoma. In October 1911, a mass appeared in the left groin, about the size of an egg.

This tumor, consisting of a mass of large lymphatic glands was removed at the Mayo Clinic on February 5, 1912. Dr. L. B. WILSON, head of the Pathologic Department of St. Mary's Hospital kindly sent me the following report :

The tumor is a pigmented sarcoma composed of medium sized round cells and oval epithelial-like cells, the latter in many areas presenting

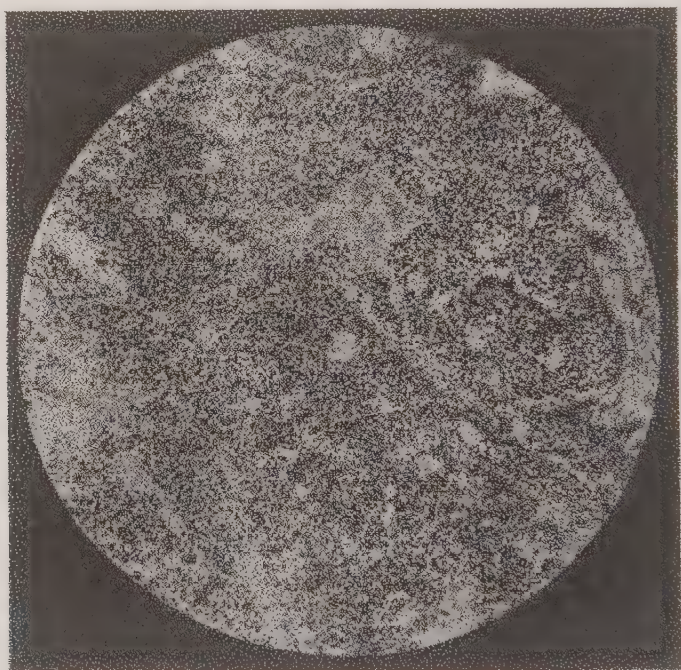


Fig. 11 (Case 80).

an alveolar arrangement. Without entering into the question as to whether these tumors are epitheliomata or sarcomata, there seems to me no doubt that this tumor was a metastasis from the neoplastic change in the pigmented mole previously removed from the fourth toe of the patient's left foot.

The patient was referred to me by Dr. W. m. J. MAYO, and physical examination on February 19, 1912, showed in the left groin a cicatrix 6 inches long extending down to the femoral region and upper

thigh, parallel with the muscles. Its central portion was unhealed for a distance of 2 inches and a deep cavity was discharging sero-purulent material. In the upper femoral region was a mass about the consistence of sarcoma, 2×3 inches in size. Apparently the growth was not entirely removed at the operation on February 5th; there was no evidence of metastases elsewhere. The patient was admitted to the General Memorial Hospital on February 20, 1912, and the mixed toxin treatment begun. All injections were made systemically into the buttocks. The patient grew very susceptible to the toxins and doses of 3 to 4 minims produced severe reactions. In a week's time there was marked evidence of improvement apparent, as shown by diminished vascularity of the growth and considerable decrease in size. At the end of one month's treatment the tumor had entirely disappeared and the patient returned to his home, with the advice that he have the treatment continued for at least six months. Whether or not this was done, I was unable to learn. The patient died on October 20, 1912, of metastases in the right hemisphere of the brain.

In spite of the fatal outcome of the case, the complete disappearance of the local, inoperable tumor under one month's treatment with the toxins, is of considerable interest especially in view of the type of the tumor, *i. e.*, a melanotic growth, probably epitheliomatous in character, which particular type has thus far been found least amenable to the action of the toxins.

CASE 81. — *Small round-celled sarcoma of the back.*

N. J., male, 8 years of age. In the latter part of August, 1901, fell from stoop, striking upon his back. Two to three weeks later, mother noticed a swelling in the left scapular region (the point where he struck), which increased rapidly in size and was soft and fluctuating almost from the start. Four weeks thereafter he was referred to me by Dr. POLHEMUS, of Nyack, N. Y. Physical examination showed a cystic swelling, the size of an orange, in the left scapular region; fluctuation well marked. Diagnosis of hematoma was made. Under ether an incision was made and a large amount of dark bluish fluid was removed with a trocar. Three weeks later the fluid returned, and there was evidence of a solid tumor in addition to the fluid. A second

operation was performed under ether, and a new growth was found which, on microscopical examination by H. T. BROOKS, Professor of Pathology of the Post Gradual Medical School, proved to be round-celled sarcoma. It was impossible, in view of the large area occupied by the tumor, to make a thorough removal. The patient was put upon the X-ray treatment shortly after the second operation. Under four months' treatment the growth had apparently disappeared. However, three weeks later it recurred and finally disappeared under the mixed toxins. The boy is perfectly well at present, twelve years later.

This patient was shown before the Clinical Congress of Surgeons of North America, in November, 1912.

My last examination was made January, 20, 1914, and the patient was in good health without any return.

Cases in which the toxins were used as a prophylactic after operation.

The following is by no means a complete list of these cases but only a few of the more interesting ones, in the majority of which it is probable the operation was incomplete and a speedy recurrence was to have been expected.

CASE 1. — *Lymphosarcoma of the axillary region.*

Mr. C. R., aged 29 years. In the spring of 1910, the patient was operated upon by Dr. SAMUEL ROBINSON, of Boston, for a tumor situated in the right axillary region. Microscopical examination showed the growth to be round-celled sarcoma. A second operation was performed by Dr. ROBINSON, on August 8, 1911, for what was supposed to be a recurrent or metastatic tumor involving the right axillary glands. The portion removed was examined by Dr. HOMER WRIGHT, Pathologist of the Massachusetts General Hospital, and pronounced lymphosarcoma. Two weeks later the patient was referred to me for toxin treatment. The treatment was started by my associate, Dr. J.-P. HOOVER, and later continued by the family physician until January, 1912, at which time there was no trace of the tumor left. I made a careful examination of the patient in October, 1913, over two years

after the treatment was begun, and found him to be in good health, with no sign of a recurrence two years after treatment.

While in this case the toxins were used chiefly as a prophylactic after operation, it is not certain that all of the diseased glands were removed from the axilla; furthermore, according to Fabian (*Münchener Medizinische Wochenschrift*, August, 1913), « there are no cases of cure by surgery on record, in which there have been metastasis, or in which the disease was no longer isolated » (confined to one glosed).

Dr. HOMER WRIGHT, pathologist of the Massachusetts General Hospital states regarding the foregoing case « I am much interested to know the outcome. This is the third or fourth case of malignant lymphoma which I have personal known to have recovered ».

Another of these cases is that reported by Dr. J.-L. GOODALE, of Boston, Mass., an inoperable lympho-sarcoma of the neck and tonsil, in which the disease entirely disappeared under the injections of the staphylococcus aureus alone (*Boston Medicine and Surgical Journal*), Sept. 1908. According to a letter of Dr. GOODALE'S, dated November, 26, 1913, the patient remains perfectly well, nearly four years later.

NOTE. — This case I believe warrants further experiments with staphylococcus toxins.

CASE 2. — *Round-celled sarcoma of the testis; toxins used as a prophylactic after operation.*

W. M. H., male 26 years, family history good. Received an injury, November, 1, 1905, followed by acute swelling, which nearly subsided, when, three or four weeks later it began to increase again. Operation performed by Dr. J.-E. SIMMONS, jr., of Omaha, in February, 1906 (three months after the trauma) which consisted in removal of the testis and cord. Pathological examination proved the disease to be round-celled sarcoma. The patient entered the General Memorial Hospital where the toxin treatment was given for two weeks, and later continued at home.

According to a letter received from the family physician, Dr. I. LUKENS (Tekamah, Nebraska) under date of Octobre, 3, 1913, the patient is « apparently in perfect health, and there is not, in any way, the slightest suggestion of his former trouble ».

CASE 3. — *Sarcoma of the kidney.*

G. D., 18 months old, weight, 21 pounds. Operation performed for sarcoma of the kidney, on August, 27, 1905, by Dr. J.-W. PERKINS, of Kansas City, Mo. Microscopical examination proved the tumor to be mixed celled adeno-sarcoma. Although the prognosis was regarded as hopeless, it was decided to give the patient a trial with the mixed toxins of erysipelas and bacillus prodigiosus. The treatment was started September, 21, 1905, under my direction and continued for two years with occasional short periods of rest, the doses ranging from $\frac{1}{2}$ to 6 minims, which usually produced a temperature of 100-101°, although sometimes it rose to 104-105°. December, 17, 1913, patient's father writes : « I am very glad to tell you that my boy is thriving in every way. He is in perfect health and there never has been any suspicion of a recurrence of the sarcoma. It is now about eight and a half years, since the operation was performed, and the toxins were started. »

CASE 4. — *Spindle-celled sarcoma of the parotid.*

Mrs. X., referred to me by Dr. W. MURRAY, of Hessle, E. Yorks, England, on March 5, 1911. In the spring of 1909 a tumor about the size of a small pea had been noticed in the centre of the right parotid. This slowly increased in size and in June, 1909, was removed by Dr. MURRAY. The specimen was sent the Clinical Research Association who reported it to be a small spindle-celled sarcoma. She was seen by Dr. CLUTTON, of London, who advised X-ray treatment which was given during July and August 1909. In May 1910 a slight recurrence was noticed which gradually increased until September 10th when it was removed by operation. In the following March (1911) when the patient was referred to me, physical examination showed the patient in good general condition. Over the centre of the right parotid there was a cicatrix about one inch long; beneath this could be felt a slight thickening smooth in outline and fixed to the deeper structures, whether it was an actual recurrence or not cannot be definitely stated. My notes read : « probably a recurrence ». The supra-clavicular and lower cervical glands are slightly enlarged. The patient was put upon small doses of the mixed toxins, the injec-

tions being chiefly made in the pectoral region. She returned to England after three weeks' treatment which latter was later continued by Dr. MURRAY. The patient grew very susceptible to the injections and the highest dose given was 2 minims. The toxins were continued with occasional intervals of rest during the entire spring and early part of the summer and a later series of injections was begun by myself while in London, in October 1911. The patient has remained in good health up to the present time. On May 9, 1913, Dr. MURRAY wrote me «The patient keeps well; there is not much room for improvement».

While this cannot be regarded as a definite disappearance of a tumor, as there was some doubt in 1911, as to whether there was an actual recurrence or not, personally I think there was and that it disappeared under the treatment. At any rate, the case may be used to illustrate the use of the toxins as a prophylactic.

CASE 5. — *Myxosarcoma of the scapular region twice recurrent, toxins used as a prophylactic against recurrence patient well nearly four years later.*

P. T., male, 39 years, referred to me on November 7, 1909, by Dr. GEORGE BREWER, for the toxin treatment in the hope of preventing a further recurrence after a second operation done for a rapidly recurring sarcoma of the soft parts in the right scapular region. The toxins were given in the neighborhood of the former growth, for three months. The patient was shown before the the Clinical Congress of the Surgeons of North America in November, 1912, and is at present in perfect health, three years and nine months after the treatment was started.

CASE 6. — *Periosteal sarcoma of the lower jaw. Apparent cure, followed by recurrence.*

A. B., female, aged 25 years. Family history negative. Several years ago a tumor was removed from the right alveolar process of the lower jaw. This returned 1 1/2 year later, for which a second operation was performed twenty months ago. A large portion of the lower jaw was resected leaving a small bridge of bone behind. The mixed

toxins (PARKE, DAVIS preparation) were used for two months before the second operation, and apparently held the tumor in check. The toxins were resumed after operation, being given three times a week, for six months, the injections being, made into the arm and buttocks. After returning home, from the second operation the treatment was given by the local physician who had no experience with the toxins and although the specific directions given upon the bottle, stated that the initial dose should be $\frac{1}{2}$ minim, by mistake, 20 minims were used and the injection was followed by a very violent reaction. The patient went into coma, in which she remained for twenty-four hours, but finally recovered. Under the severe reaction, the small bridge of bone was broken, causing a bad deformity in the chin. The toxins were again resumed and continued in moderate doses for an entire year. The patient consulted me in April 1908, two years after the last operation. Physical examination at this time showed her general health apparently good; there was a marked deformity of the lower jaw, the broken portion of the centre of the lower jaw overlapping considerably. I failed to find any signs of a recurrence and advised discontinuing the toxins, believing that she would have no further trouble. — In March 1912 she again consulted me, nearly four years later, with marked evidence of local recurrence. She was under my care for several months but both toxins and X-ray had little effect in checking the growth.

CASE 7. — *Sarcoma of little finger. Disappearance under two months toxin treatment. Patient well.*

G. J., 21 years old. First noticed a small swelling on the outer portion of the little finger early in 1907. First operation February, 1909. A portion of the tumor removed under cocaine, proved to be sarcoma, apparently starting in the fascia or periosteum, of the giant-celled type; a more extensive removal was then made under chloroform. When I first saw the patient on April 3, 1909, there was considerable thickening in the region of the scar; flexion limited to one-half. The patient was put upon systemic injections of the mixed toxins of erysipelas and bacillus prodigiosus and the treatment continued for two months, two or three times a week. The doses were carried up to the point of causing a very slight temperature and

malaise, but no chill. Occasional examinations since this time, the last one in January, 1911, have shown the finger perfectly normal, motion normal; the scar is soft and pliable.

CASE 8. — *Round-celled sarcoma of undescended testis.*

D. E. B., male, 37 years, referred to me by Dr. JOHN B. MURPHY, of Chicago, in July, 1908, Family history negative. Patient has had tuberculosis of the left lung for the last ten years; left undescended testis from birth. By the end of May, 1908, he first noticed dull pain in the left hip and inguinal region. Operation by Dr. JOHN B. MURPHY, June, 11, 1908 who removed the sarcomatous undescended testis which had reached the size of a fist. The disease was pronounced round-celled sarcoma, which diagnosis was confirmed by Dr. JAMES EWING, pathologist of Cornell University Medical School. The patient was sent to me in July 1908, for prophylactic treatment. His condition at that time showed no loss of weight, a recent incision in the left iliac region, considerable induration, but no distinct tumor. The patient was immediately put upon the mixed toxins in gradually increasing doses up to the point of obtaining good reactions. The patient proved very susceptible, in one instance a temperature of 106° followed the injection of 3 1/2 minims. After leaving the hospital, the patient was strongly advised to continue the treatment in small doses for a long period, but on account of the tuberculosis of his lung which necessitated his living in Wyoming, no further treatment was carried out. In a letter of November, 15, 1909 he stated that there was no recurrence, but he was having increasing trouble from his tuberculosis of the lung. He died in the early part of March, 1912, possibly from a metastatic recurrence, although it is not certain that death was not entirely due to tuberculosis.

CASE 9. — *Periosteal sarcoma of the femur following trauma; hip joint amputation with subsequent treatment with the mixed toxins of erysipelas and bacillus prodigiosus. Well more than two years.*

H. P., male, 27 years. Good family history. Patient received an injury to the upper part of his left femur, in October 1912. Two to three weeks afterward he began to have pain in this region, but noticed

no enlargement until January 1912, when he observed a fusiform swelling in the upper part of the femur. This rapidly increased in size accompanied by marked deterioration in general health. The patient was referred to me by Dr. WILLIAM L. BRADLEY, of this city and I first saw him on March 28, 1912. He had at that time been confined to his bed for two to three weeks, suffering severe pain. Physical examination showed a man, markedly emaciated and cachectic. Examination of the left femur showed a fusiform enlargement occupying the whole upper half of the thigh, the largest circumference measuring 22 inches. The tumor extended well beyond Poupart's ligament anteriorly, and posteriorly above the trochanter. The joint was apparently not involved and there were no glands in the groin. The skin was not adherent but was of purplish color, due to a large number of dilated veins, I could find no evidence of internal metastases. The patient was referred to the General Memorial Hospital and in spite of the great extent of the disease, I believed it worth while attempting an amputation at the hip joint, which was performed on the following day, April 1, 1912, Wyeth's pins were used but the growth extended so high up that after the leg was removed, the muscular tissues retracted underneath. An incision was made over Scarpa's triangle and artery and vein were first tied; the skin dissected back above Poupart's ligament and above the trochanter behind. Although there was very little loss of blood, the patient's general condition was extremely bad and when the operation was completed, he was practically pulseless, so that it was doubted he would live to go back to the ward. He was given 4 ounces of black coffee and whiskey per rectum, and on reaching the ward 1,000 c. c. of salt solution intravenously. He rallied shortly afterward and was in good condition the following morning; he has made an uninterrupted recovery. Dr. EWING's report reads: « Myxo-chondrosarcoma, the cartilage is almost completely degenerated into mucous tissue and there is some well-defined embryonal cartilage. » The mixed toxins were begun as soon as the patient had sufficiently recovered from the operation, and continued for three months, during which time the patient's general condition rapidly improved. He was shown before the New York Surgical Society May 8, 1912, about one month after operation, and again before the Clinical Congress of Surgeons of North America, in November, 1912, in perfect health without any trace of a recurrence; he had gained

30 lbs. in weight. My last examination was made December 2, 1913, and he was in excellent health, normal weight, and no evidence of recurrence two years later.

Cases of inoperable carcinoma treated with the toxins.

CASE 1. — Inoperable epithelioma of the chin, lower jaw, and floor of mouth; patient well without recurrence six years later.

Mrs. W., aged 34 years. Patient was admitted to the Methodist Episcopal Hospital of Brooklyn in May, 1894, with a rapidly growing tumor involving the central portion of the lower jaw, the floor of the mouth, and the soft parts of the chin. There was an area the size of a silver half-dollar upon the chin, which was the seat of a typically epitheliomatous ulcer. A portion was removed and pronounced by the pathologist epithelioma. The tumor had started four months previously. Dr. GEORGE R. FOWLER of Brooklyn regarded the case as inoperable and without hope. He stated that the only operation that could be done would be removal of the lower jaw, floor of mouth, and a part of the tongue; that the risk of death from the operation would be great, and that recurrence within a few months would be almost certain. He referred the patient to me for treatment with the toxins. In view of the tumor being epithelioma I gave a very bad prognosis, but promised to try the injection.

She was admitted to the New York Cancer Hospital early in June, 1894, and was treated with the unfiltered, mixed toxins, for about ten weeks. The injections were made into the chin and repeated daily, as a rule. In three weeks the ulcerated area had entirely healed, and the diseased portion in the floor of the mouth had greatly improved.

In September, 1894, the patient had become very much run down from the long-continued injections and severe reactions, and two small ulcers $\frac{1}{4}$ inch in diameter appeared in the chin. She was sent home to recuperate. Her only treatment consisted in the administration of tonics and the local application of electricity to the chin for a short time by Dr. SARAH V. BURNETTE. The tumor entirely disappeared.

She was examined by a number of surgeons, December 14, 1895. No induration could be detected in the scar nor in the floor of the

mouth, and the patient was still well when last heard from, six years later.

Pathologist's report. — « Material from chin and lower jaw, May 20, 1894. Sections were not entirely satisfactory, but from gross appearance of the materials and those revealed by the microscope the diagnosis of epithelioma is offered. » — DR. WILLIAM N. BELCHER, pathologist to the Methodist Episcopal Hospital, Brooklyn.

Dr. FOWLER, in his letter enclosing the pathologist's report, stated :

While I am sure that the case was one of epithelioma, judging from the clinical standpoint, and based upon the history of its rapid growth as well as its recurrence upon removal, yet I am fully aware that epithelial findings, from every standpoint, should be absolutely beyond question.

Dr. WILLIAM N. BELCHER, pathologist to the Methodist Episcopal Hospital, and member of the Brooklyn Pathological Society, made the report, and in a letter explaining his report he states :

The fragments were frozen by the use of the carbon-dioxide apparatus, and freehand sections made. Notwithstanding the unsatisfactory picture revealed by the microscope there seemed to me to be sufficient to warrant the opinion that the material was of an epitheliomatous character. Upon consulting the hospital records, I find that the diagnosis of epithelioma was made by the operating surgeon, presumably prior to my report, and it would seem to me to be as nearly correct as any diagnosis can be.

CASE 2. — *Carcinoma of both breasts ; amputation ; inoperable recurrence in the pectoral region with extensive involvement of supraclavicular and cervical glands. — Entire disappearance under prolonged treatment with the mixed toxins of erysipelas and bacillus prodigiosus. Patient in perfect health at present five years later.*

Miss E. J. D., age 39 years. Family history. Paternal aunt died of cancer of breast fifteen years ago when 84 years of age.

Constant irritation of the breast from aluminium corset which she wore for severe curvature of spine; had bad fall when five years old. At six developed infantile paralysis followed by very bad lateral curvature and as a worn braces and corsets ever since the fifteenth or

sixteenth year. The patient noticed a small swelling the size of a pea in the left breast five years ago; occasional slight discharge from nipple; pain during the past year has been sharp and stinging in character. Physical examination showed a small nodule, not larger a pea, in the upper part of the left breast, not attached to the deeper parts; skin freely movable.

Clinical diagnosis. — Fibroadenoma. Removal under cocaine. Microscopical examination by Dr. CLARK : fibroadenoma. No evidence of malignancy. One year later a small nodule appeared in the immediate vicinity of the first, which was also removed. At this time a more extensive operation was done under ether anæsthesia. The tumor seemed the same, clinically, as the first : fibroadenoma. Microscopical examination at this time showed the main tumor fibroadenoma, but there was a small area in which a carcinomatous change had taken place. Another operation was performed a week later, and the entire breast was removed; axilla not opened; pectoral muscles not removed, it being important not to prolong the anæsthesia on account of her general condition. One year later a similar nodule appeared in the right breast at about the same location. This was also discovered when exceedingly small, hardly larger than a buckshot. The nodule seemed slightly harder than those in the other breast and the skin showed the faintest evidence of beginning adhesion.

Amputation of the entire breast, without opening the axilla, was performed February, 1908. Patient made a good recovery.

Microscopical examination by Dr. JAMES EWING showed typical carcinomatous changes in the small nodule.

In December, 1908, she again consulted me and I found a well-marked recurrence in the pectoral region with considerable involvement of the glands in the left cervical region. The case was clearly inoperable, and as an experiment I tried the thyroid preparation made by Dr. S. P. BEEBE of the Cornell University Medical School, for a few weeks. The tumors continued to increase in size in spite of treatment and when I again examined her, in February, 1909, there was a hard, carcinomatous mass occupying the entire left pectoral region with involvement of the cervical glands from the clavicle nearly to the mastoid. As the trouble was clearly carcino-

matous, I gave the family an absolutely hopeless prognosis and stated that I did not believe the patient could live beyond six months. I was asked if it would be of any use to try the toxins in such a case and I replied that nothing more could be gained than possibly some slight retardation of the growth, that there was no hope of a cure. In spite of this the sister was very anxious that the treatment should be tried. In order to lessen the discomfort associated with the treatment, due to the local irritation of the injections, I directed her family physician, Dr. W. J. BOTT of Palmyra, New York, to use only he filtered toxins, which are about half the strength of the unfiltered, and very much less irritating. The patient proved exceedingly susceptible to the toxins, which were started with $\frac{1}{2}$ minim dose and gradually increased to 3 minims; very small doses, however, were sufficient to produce moderately severe reactions. Within a few weeks her physician wrote me that very marked improvement had occurred and that the tumors were steadily decreasing in size; the improvement steadily continued, and by August, 1909, Dr. BOTT wrote me that both pectoral and cervical tumors had practically entirely disappeared. I examined the patient personally on February 24, 1910, at which time I could find no trace of a tumor in either pectoral or cervical region. The patient regained her normal health and never felt better; there were no glands in the axillæ and no swelling in the arm. Up to this time she had received 104 injections ranging between $\frac{1}{2}$ and 3 minims. Although she objected strongly to a continuation of the treatment, I succeeded in persuading her to go on with it, and it has been continued, with occasional intervals of rest, up to February, 1911. Her acute susceptibility to the toxins not only persisted, but became increased so that toward the end she was hardly able to take more than 1 and $\frac{1}{2}$ minims. My last examination of the patient was made March 30, 1914; I found her still in good health; no trace of a tumor could be felt in either pectoral or cervical regions, more than five years after treatment was begun, and the patient was last shown by me before the New York Surgical Society on March, 1912, three years after treatment.

This case is perhaps the most important in the entire series, as it shows the curative effect of the toxins in a case of inoperable carcinoma, with the diagnosis established beyond any question.

CASE 3. — *Adenocarcinoma of the soft palate. Inoperable; rendered operable by the use of the mixed toxins.*

W. D., 52 years of age, referred to me by the late Dr. WM. F. DUDLEY, of Brooklyn, on June 1, 1912. The patient had always been well until six months before, when he first noticed a swelling just behind the soft palate. This was treated by Dr. DUDLEY, but the growth continued to increase in size under local treatment. Physical examina-

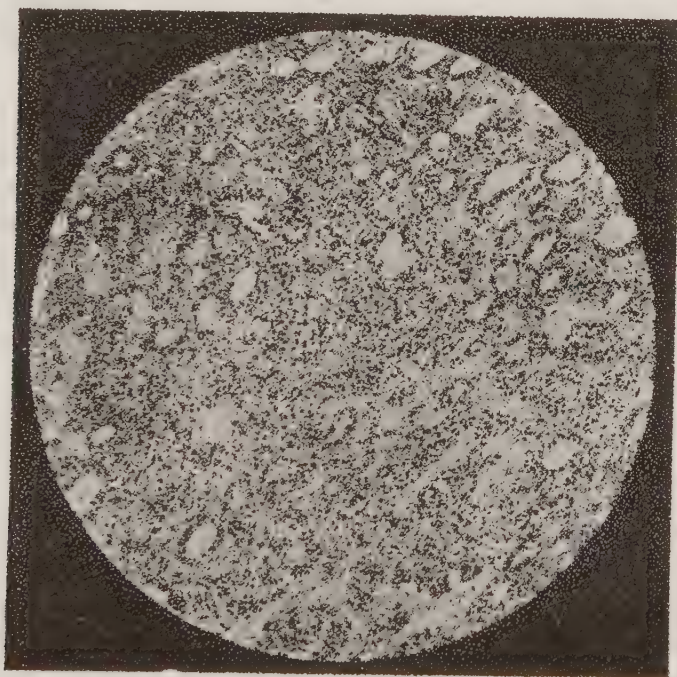


Fig. 12 (Case 3).

tion by myself in June, 1902, showed the soft palate pressed forward and distinctly bulging into the cavity of the mouth. The space behind the palate was practically filled up by the large tumor, interfering considerably with speech and swallowing. On palpation a smooth, rounded tumor was found, moderately firm in consistence, situated behind the soft palate and extending backward, but point of origin not ascertainable. He entered my service at the General Memorial Hospital two days later, and was put upon the injections with the

mixed toxins, systemic at first (pectoral region). At the end of a week an exploratory incision was made in order to obtain material for microscopical examination. Dr. EWING's report reads as follows :

I think the tumor of the palate must stand as an adenocarcinoma. It is made up of small alveoli lying in hyaline or mucoid struma. Most of the alveoli are intact, some are carcinomatous and diffuse. The tumor probably arises from the mucous glands of the palate. It is not at present very malignant and a thorough extirpation ought to cure.

The mixed toxins were continued locally and systematically. The tumor showed marked diminution in size and became less diffuse and more discrete, so that its outline could be more easily defined. The tumor also became harder in consistence so that a needle entered with difficulty. The local injection produced fairly severe reactions, a temperature of 102 to 104° being obtained with $\frac{1}{3}$ to $\frac{1}{2}$ minim doses. In view of the decrease in size of the tumor, on August 1, 1912, under ether anesthesia and after preliminary ligation of the external carotid, I attempted to remove as much as possible of the tumor, making an oblique incision 2 $\frac{1}{2}$ inches long, through the soft palate. A tumor, fairly well encapsulated, was found, about the size of a small egg. It extended backwards and downwards for about 2 inches. It was found impossible to remove the capsule, and curette and scissors had to be employed. A second examination made by Dr. EWING confirmed the diagnosis of adenocarcinoma, already made at the time of the first examination. The wound healed very rapidly and the patient was sent to the country for two weeks to recuperate, after which he resumed his occupation.

Physical examination on July 1, 1913, shows nothing but scar tissue at the site of the wound. The toxins have been continued by his family physician twice a week since, but in no way interfering with his work. His general condition is good and he weighs more than at any previous time.

Last examination made January 10, 1914. There is no trace of return or of any induration at site of tumor, and his general health is excellent. The toxins were kept up for more than a year.

CASE 4. — *Recurrent epithelioma of face.*

X., male, 45 years of age. The patient had a small, recurrent epithelioma of the face, involving the lower eyelid. The primary tumor I had removed by operation at the New York Cancer Hospital, eighteen months before and microscopical examination by Dr. E. K. DUNHAM, pathologist of the hospital, proved the growth to be epithelioma. Although the tumor in this case was not extensive, its removal by operation would have necessitated enucleation of the eye, and since he had lost the other eye in youth, I decided to try the toxins before sacrificing the eye. The recurrent tumor was treated at the hospital in February and March, 1895, with the result that the growth apparently disappeared. In January, 1896, when last heard from, there had been no return of the disease. The later history I have been unable to trace.

The following case, I believe, adds considerably to the evidence in favor of the toxins as a prophylactic.

CASE 5. -- *Epithelioma of the lower eye-lid with involvement of the orbit. Recurrent after three operations; the mixed toxins used as a prophylactic, continued for nearly two years; patient well at present, over three years.*

R. J. H., 38 years of age, male, veterinary physician. In November, 1909, first noticed a pimple in the middle of the left lower eyelid which apparently started in the skin, rather than in the mucous membrane. It grew rapidly and was first treated as a sty. On December 13, he had four to five treatments with the violet rays with the result that the tumor grew more rapidly.

He was advised to have a portion removed for microscopical examination. This was done and the pathologist pronounced it hyperplasia, without trace of malignancy. The patient then saw a dermatologist who, relying on the correctness of the pathologist's report, treated it as a granuloma. Physical examination by myself on February 24, 1910, showed a tumor occupying the entire lower eyelid, extending upwards and completely closing the eye. The tumor was flat, very slightly protuberant, covered with sluggish granulations having the typical appearance of epithelioma, which was the clinical

diagnosis made. The following day I removed the entire eyelid. Microscopical examination by Dr. James EWING. Showed it to be Epithelioma.

Two weeks later, the disease recurred in the inner canthus of the eye, extending partly into the orbit. A second, thorough operation was done followed by small doses of the toxins. A month later, another recurrence was noticed; this grew very rapidly and I removed the eye. In the latter part of April, 1910, there was again a local recurrence at the bottom of the orbit which was scraped out by my associate, Dr. WM. A. DOWNES, in my absence. The toxins were continued regularly; the doses were pushed to the point of tolerance and the injections were continued for one and-a-half year, with occasional intermissions. The patient proved exceedingly susceptible, never taking more than 2 minims. He remains perfectly well at the present time, four years later.

CASE 6. — *Epithelioma of the superior maxilla, showing marked inhibitory action of the toxins.*

W. C., female, 65 years of age. Family history good. The patient first noticed trouble in the left superior maxilla in Decembor 1910 and was treated by a dentist for what he called « cystic tooth ». It came on shortly after the extraction of a tooth from which the jaw was considerably bruised. The swelling gradually increased in size. The patient was under treatment of Dr. JOHNSON, of Hartford, Conn. who used the toxins and under date of March 5, 1911, wrote me as follows :

The case of Mr. W. C. is a very interesting one. The malignant growth was located at the angle of the superior maxilla and extended along the mucous membrane of the roof of the month. This location rendered it inoperable. When she came to me, the process of necrosis was well-marked. No microscopical examination of the growth, I diagnosed it as a sarcoma. The fact that it yielded se readily to the toxin treatment I think, corroborated my diagnosis.

I gave her an injection into the mucous membrane in close proximity to the growth, and some times into the growth itself for a period of four weeks. At this time the malignant growth had entirely disappeared and the site of the growth leaving but little trace of its

former location. Up to date there has been no sign of a return of the growth.

Although the toxins were continued in small doses by Dr. JOHNSON, on April 21, there was evidence of a slight recurrence, and on June 19, 1911, the patient was referred to me. Physical examination at this time showed two thirds of the left superior maxilla and hard palate occupied by a tumor projecting into the cavity of the mouth about $\frac{3}{4}$ inch., smooth and soft in consistence; the mucous membrane was more vascular than normal, but unbroken, except that there was a small area, the size of silver quarter, which was ulcerated. There were no enlarged glands and no exophthalmus. The injections were continued under my direction by my associate, Dr. HOGUER, and partly by myself during the summer and fall of 1911. She was later admitted to the General Memorial Hospital where she remained until.

She proved very susceptible to the toxins and was never able to take over 2 to 3 minims without severe reaction. The growth was unquestionably held in check by the toxins, but when they were discontinued for any period of time, there was again increase in size. In the early part of 1912 several enlarged glands were noticed. From the consistence of the glandular swelling as well as the general characteristics of the tumor of the jaw, I made a clinical diagnosis of epithelioma, which was confirmed by microscopical examination by Dr. EWING. In the summer and fall of 1912, the tumor slowly increased in size, accompanied by a good deal of pain and her general health slowly failed. The toxin treatment was abandoned in May 1913 and she died on September 21, 1913.

The case is interesting from the fact that the original tumor disappeared under the toxins and that the recurrent growth was almost completely held in abeyance for a long period, by the toxin treatment.

(For a more complete history of the following two cases, see my previous paper on The Treatment of Inoperable Sarcoma with the mixed toxins of erysipelas and bacillus prodigiosus. — *Journal of the American Medical Association*, August 27, 1898.)

CASE 7. — *Inoperable carcinoma of the breast, three times recurrent; toxin treatment for two and one quarter years; disappearance of tumor, followed by local and general recurrence.*

Mrs. B., aged 40 years, was first operated upon for a primary carcinoma of the right breast, in January, 1894, by another surgeon, who did a partial excision of the breast, not opening the axilla. In the latter part of the same year, there was a well-marked recurrence, local and axillary. I performed the second operation at the New York Cancer Hospital, in June 1895. The axilla was found to be so extensively involved that it was impossible to remove all of the diseased glands, and a gland the size of a large hickory-nut, located high up in the axilla and completely surrounding the vein, was left behind. Local recurrence took place in the center of the cicatrix before the wound had entirely healed, and the disease progressed rapidly. The arm soon became oedematous. I decided to try the effect of the mixed toxins, expecting little more than a temporary retardation. The injections were immediately begun; so signs of retrogression. The local tumor was removed and the toxin treatment continued. Local recurrence quickly followed but under larger doses of the toxins, and more frequent injections, the carcinomatous ulcer finally healed and the tumor in the axilla decreased so that it could no longer be felt. The swelling of the arm, which at one time was two inches larger than the other, became much reduced so that there was only one-half inch difference. Patient gained ten pounds in weight. She remained well until the summer of 1897, when a local recurrence developed, which was soon followed by signs of metastasis in the liver. Death occurred in December, 1897.

CASE 8. — *Recurrent double carcinoma of the breast.*

Mrs. W., aged 56 years, first noticed trouble in the left breast in the year, 1891. One year later she noticed a similar condition of the right breast. The first operation, double amputation of the breast, was performed by Dr. MAURICE H. RICHARDSON, of Boston, on October 8, 1895. Extensive local recurrence took place the following June, consisting in a mass involving the entire thickness of the skin over an area four inches in diameter. She, being opposed to further

radical operation, I advised local excision of the affected area, to be followed by the use of the mixed toxins in the hope of delaying a recurrence, although I did not believe it possible to effect a cure. Excision was performed by Dr. RICHARDSON and before the wound had entirely healed, new nodules appeared in the outlying skin near the anterior axillary line. The toxins were begun January 10, 1897, and continued with occasional intervals of rest for two years. The patient recovered her general health although occasional small nodules the size of a split pea occurred from time to time beneath the skin. These were removed under cocaine, and the toxins continued. The patient remained in fairly good health for eight years, and then died of intra-abdominal metastasis.

Final results. — Since I began my investigations in 1891, I have treated 710 patients with the mixed toxins of erysipelas and bacillus prodigiosus. These cases were all inoperable, and in the majority, recurrence had taken place after one or more operations. The few exceptions, which were not strictly inoperable, were cases of sarcoma of the long bones, in which operation entailed the sacrifice of the limb, or lower jaw.

Of this total number (710) 80, or little more than 10 per cent, have been successful — by successful, I mean the disappearance of the tumor and restoration of function, and health. In the great majority of cases in which the tumor disappeared under the toxin treatment, the cure has remained permanent, and in a certain number, a recurrence either local or general, has taken place after a period varying from a few months to eight years.

My own series of cases show that in eleven instances definite recurrence took place after an inoperable malignant tumor had once disappeared under the toxins. All of these (ended fatally with two exceptions in which) the disease was again controlled by further use of the toxins.

Final results. — Of my personal cases successfully treated with the toxins, 59 remained well over three years, namely :

13 well from	15-20 years
5 — —	10-15 years
25 — —	5-10 years
16 — —	3-5 years

28 have remained well less than three years, *i. e.* :

15 well from	2-3 years
8 —	6 months to 1 year
5	less than six months

Report of a few of the more important.
Cases treated by other men.

CASE 1. — *Melanotic sarcoma of rinht posterior triangle of neck.*

Mr. J. B. Patient of Dr. GREENWOOD (Hill Crest, Cardigan Lane, Leeds, Eng.) Microscopic diagnosis : Melanotic sarcoma. Incomplete operation was performed, followed by a recurrence. Patient's condition fairly good, no pain, no cachexia. Temperature normal, size of growth $2\frac{1}{2} \times 3$ inches. March 3, 1911 (eight days after recurrence) patient was put upon the mixed toxins (Coley's sent by the Huntington Fund); initial dose being $\frac{1}{2}$ minim. This was gradually increased to 10 minims. He received in all thirty-six injections (between March 3, and July 11, 1911) which were made in the neighborhood of the recurrence. In the beginning, the treatment was given with intervals of one to two days, later, three days. As regards usual reactions, Dr. G. states that in one-half hour, temperature rose to about 101° which was sometimes followed by a rigor varying in severity. There was generally a brawny induration at the site of the injections lasting for about a week. Improvement was immediate, the tumor starting to shrink, until on July 11, 1911 there was no trace of the disease left. Injections continued. Patient shown before Leed's Medical Society (see *Lancet*), January 19, 1912, well.

Hill Crest, Cardigan Lane,
Leeds, England.

July 16, 1913.

DEAR DR. COLEY,

I shall be very glad to be of service to you, and send you the following data :

A. — Mr. B. is in splendid health, doing full work and now weighs 12 lbs. more than he did in March, 1911, when he first came under

treatment. There is no sign of recurrence locally, nor are there any enlarged glands. He still has anaesthesia over the deltoid, the result of severance of the superficial cutaneous nerves. The site of the tumor is marked by a hollow covered by clean scar, with no trace of pigment.

B. — His injections were spread over the period, March 1911 to April 1913 (two years., one month). In all he had 105 injections — the highest dose was 15 minims; during the middle portion of the treatment, April to August 1911, an average dose of 10 minims thrice and then twice weekly was maintained; then to January 1912, 10 minims once a week then during the whole of 1912, one dose weekly of 5 minims.

C. — The giving of *nux vomica* had an unmistakably beneficial effect.

D. — Three months after commencing treatment he was doing his ordinary work except on his « injections » days, when he was granted a half day holiday — evidence that the treatment does not altogether cripple the patient's earning powers.

E. — The report of the pathologist was so precise, and the clinical features so unmistakable, that the patient's life was quite despaired of, and there was neither tumor nor slide kept — it is a pity. The treatment was only used (without faith) to convince the relatives that every means had been tried.

F. — There have been two more successful cases of ordinary sarcoma cured by the treatment, shown at the Leeds Medico-Chirurgical Society, since March, 1911.

G. — The severity of the reaction was very precise and could be prophesied exactly :

1. The nearer the neck the quicker and more severe the reaction.
2. The longer the interval the quicker and more severe the reaction.
3. Only when the injections were daily and steadily increased did anything like accumulative effect occur and then it seemed rather that the patient had not had time to recover his strength.

H. — The reaction usually lasted about two to four hours according to the dose — but immediately the sweating stage was over he got up and ate a hearty meal.

Yours sincerely,

(Signed) H. HAROLD GREENWOOD.

CASE 2. — By Major C. G. SPENCER of the Royal Army Medical Corps. (*Trans. Royal Society of Medicine*, 1909, and *Journal of the Royal Army Medical Corps*, 12, 1909, p. 449.)

Inoperable sarcoma of the abdominal wall successfully treated with the mixed toxins. Patient well more than four years afterwards.

Male, 33 years of age, was admitted to the hospital at Bulford, July 21, 1909. Examination showed a hard tumor in the lower portion of the abdomen; it extended from the pubic bone upwards to to 1 and 1 $\frac{1}{2}$ inches of the umbilicus, 3 inches broad; firmly attached to the bone, but evidently originated in the abdominal wall. September 5, 1906, an exploratory examination was performed and a portion of the tumor removed for microscopical examination, which showed it to be a spindle-celled sarcoma. An unsuccessful attempt at removal was made a week later. On September 22nd the Coley's toxins were begun and given every other day, twelve injections in all and three minims being the highest dose. The treatment was then discontinued as there had been no appreciable improvement and the patient's general condition was greatly impaired. On his return from a two months' furlough, striking improvement was apparent; he had gained fifteen pounds in weight, and was again able to walk and take exercise without discomfort. The tumor was distinctly smaller and softer. A second course of toxin treatment was begun December 16, 1906, and continued until January 11, 1907, fifteen dose ranging from 1 to 6 minims being given. His general condition again deteriorated and on January 21st he was sent on a month's furlough with the same favorable result as before. He was subjected to a third series of injections of six minims each from February 23rd to March 28th, and discharged from the hospital on April 3rd, when the tumor had entirely disappeared, but a mass could still be palpated per rectum.

Under date of June 27, 1913, Dr. SPENCER writes :

The above case was well when last I heard, about a year ago.

Second case of Dr. SPENCER (reported in the *Journal of the Royal Army Medical Corps*, June, 1913, and *Lancet*, December, 21, 1912).

CASE 3. — *Lympho-sarcoma treated with Coley's fluid.*

Corporal M. M., aged 25, was first seen by Dr. SPENCER in February, 1912. A swelling in the left side of the neck had been noticed by the patient a year previously, since when it had slowly enlarged. On admission there was found a soft, rounded, freely movable tumor beneath the left sterno-mastoid. This was excised on March 6, 1912, and sent to the Royal Army Medical College for examination. Recurrence took place very rapidly, the left side of the neck becoming filled with masses of enlarge glands. The pathological report was that the tumor was a lympho-sarcoma. On March 29 an attempt was made to clear out the posterior triangle on the left side, but removal of the growth was incomplete. The wound healed well, but again recurrence took place very quickly.

Treatment with COLEY'S fluid was commended on April 6th, PARKE, DAVIS & Co's preparation being used. The initial dose was $\frac{1}{2}$ minim, and this was gradually increased for three weeks, an injection being given almost every day. By April 26 the amount given daily was 10 minims, and this amount was continued until May 11

A well-marked reaction with a good deal of local inflammation followed each injection. Except for the first few days, all injections were made into the tumor itself. After the first week of the treatment no further increase in the size of the growth could be made out, and decrease in its size soon became apparently though this was masked to some extent by the local inflammation and thickening set up by the injections. After the injections were suspended on May 11, the inflammatory swelling subsided, and in a few days nothing could be felt of the tumor. A further course of injections was given from May 29 to June 29, 10 minims being given on alternate days. The patient was kept under observation for two months, and then returned to duty. When last seen, in March, 1913, there was no sign of any further recurrence, and, except for the fact that at the second operation the spinal accessory nerve was injured, causing some weakness of the shoulder, he appears to be in perfect health.

Summary of treatment. — Initial doses, $\frac{1}{2}$ to 9 minims, April 6 to 25, 16 injections; total 76 minims. Full doses, 10 minims, April 26 to May 11, 14 injections; total, 140 minims. Second course of

injections, 10 minims, May 29 to June 29, 15 injections, total, 150 minims. Patient was seen in June 19, 1913, at which time he was in perfect health.

CASE 4. — *Adeno-carcinoma of ovary.*

Case of Dr. ARTHUR D. WHITE (Ithaca, N. Y.) and Dr. ROBERT T. MORRIS (N. Y. City).

Mrs. G. In the early part of December, 1912, Dr. MORRIS operated for a large intra-abdominal tumor originating in the pelvis, which



Fig. 13 (Case 4).

was believed to be a malignant parovarian cyst. The tumor weighed upwards of 10 pounds; owing to some involvement of the mesentery and intestine it was impossible to make a complete removal. Dr. MORRIS told the family definitely that there would be a speedy return. Dr. H. B. BESEMER of Ithaca, examined a specimen of the portion removed, and his tentative diagnosis reads : sarcoma.

A recurrence followed almost immediately after the operation, and increased rapidly in size. At the end of 3 weeks a large mass could be felt, reaching from the pelvis nearly to the naval, causing bladder symptoms. The patient's general condition was also rapidly deteriorating. December 26, 1912, Dr. MORRIS was again called in consultation and pronounced the case hopeless as far as surgery was concerned, and called me up to ask my opinion as regards the use of the toxins. I stated that I believed the prognosis very grave, but if the disease was sarcoma I would strongly advise the use of the toxins, before abandoning the case as hopeless. I wrote Dr. WHITE immediately giving him careful directions about carrying out the treatment, and had some toxins sent him from the Huntington Fund Laboratory. On January 13, 1913, he wrote me that the tumor had very much decreased in size since the treatment was begun. A slide of the original tumor was forwarded by Dr. BESEMER to Dr. EWING, who gave the following report, dated January 23, 1913 :

Section is composed of desue fibrous tissue in which lie rather numerous groups of epithelial alveoli. There is *no trace of sarcoma*. Probable diagnosis : *Infiltrating Carcinoma*.

In view of the difference in opinion expressed with regard to the diagnosis, I sent for some of the original growth, which fortunately had been saved, and this was submitted to Dr. EWING, whose second report reads :

Section shows a tumor process which I interpret as a papillary adenocarcinoma arising from the pelvis of the kidney. The structure varies greatly. In places, there was cystic alveoli, adeno-carcinoma, and fibro-carcinoma. There are areas of fibrosis, areas of necrosis, and much fibrous muscular tissue.

Dr. MORRIS's last report of March 20, 1913, reads :

Mrs. G. is doing remarkably well. The large rapidly growing mass immediately began to subside under the influence of your toxins, and there is now practically nothing left.

April 13, 1913, Dr. MORRIS writes :

The toxins were begun January 4, 1913, with a very rapid disappearance of the mass. Thirty-five injections have been given to

date, ranging from seven and a quarter to thirteen drops. She is now getting ten drops three times a week. Patient is doing nicely. Aside from slight abdominal tenderness there is no sign of her disease. It certainly was startling to see the subside under the toxin treatment. The patient remained well during the summer and fall of 1913.

A letter just received from Dr. Waite states that the patient died of acute nephritis on January 13, 1914. The toxins had been given for over a year with only one interval of three weeks' rest. It is possible that the nephritis was caused by the continued administration of the treatment in such large doses.

CASE 5. — *Dr. Hundley's case. Spindle-celled sarcoma of the uterus.*

Mr. A. C., 38 years, two children, last child in 1893 (referred by Dr. J. M. HUNDLEY, of Baltimore). Patient first noticed trouble in the fall of 1902. Consulted family physician who made a diagnosis of myoma. In December, 1903, she was operated upon by Prof. J. M. HUNDLEY, who supposed the trouble to be an ovarian cystoma and uterine fibroid, the size of a foetal head. Supra-vaginal hysterectomy was done, leaving the cervix. Microscopical examination made by Dr. J. L. HIRSH, December 23, 1903, proved the supposed fibroid as well as the entire uterus, to be a round and spindle-celled sarcoma. January 15, Dr. HUNDLEY attempted to remove the cervix, but had to give up on account of patient's weak heart action. At this time, he detected a tumor in the right lateral fornix, apparently spring from the broad ligament, pelvic bone, and fascia, undoubtedly sarcomatous in character.

January 22, 1904, he began to use the mixed toxins, injecting alternately directly into the cyst and cervix, through the vagina. The tumor in both regions almost immediately began to diminish in size and finally disappeared entirely. In a letter dated September 27, 1904, Dr. HUNDLEY stated that to all outward appearances, the condition was normal. She received thirty-three injections in all.

I have personally examined the patient many times since, when she was in perfect health, of normal weight, and careful vaginal examination showed no trace whatever of any growth. Patient has remained well ever since, and I found her in perfect condition on March 9, 1912.

She was still well July 1913, ten years later.

CASE 6. — *Sarcoma of the kidney involving the retroperitoneal glands.*

Patient of Dr. H. K. McDONALD (Halifax, N. S.) and Dr. A. S. BURNS (Kentville, N. S.).

The following history of the case is given by Dr. McDONALD, the attending surgeon, and Dr. BURNS, later carried out the toxin treatment :

M. P., female, 27 years old. History of rapidly deteriorating health, since the early part of 1912. She consulted her family physician, who, on examination, in the latter part of August, found a large mass in the ilio lumbar region? She was taken into Halifax (she living in the Annapolis Valley about 100 miles distant) and was then seen by Dr. McDONALD and Dr. JOHN STEWART. It was decided to do an exploratory operation : a loin incision was made and the kidney exposed. The upper and middle third of the latter were found apparently normal : the lower pole was occupied by a large tumor which was adherent to a much larger growth anteriorly. Section of the tumor was removed for microscopical examination. The patient was then turned upon her back and a laparotomy made, the same disclosed a large retroperitoneal mass which it was quite impossible to remove. Examination of the section of the growth by Dr. W. A. LINDSAY, Pathologist to the Hospital, showed it to be round-celled sarcoma.

The patient made a very poor operative recovery. A sinus developed at the site of the incision in the loin. She was looked upon as entirely hopeless and was removed on a stretcher and special car to her home? Dr. McDONALD states that no-one believed she would live to get to the end of her journey; two weeks later she was put upon small doses of the mixed toxins. Dr. McDONALD stated the condition at that time was so bad that the toxins were used as a last resort, and he thought that « if they were of no benefit, they would perhaps have the other effect and put the patient out of her misery ». This, it should be stated was with the full consent of the parents. After the first injection, Dr. McDONALD states, she began to improve. When the dose of four minims had been reached, the sinuses in the lumbar region closed. The tumor began to show marked decrease in size, and after eighteen injections had been given the family physician Dr. BURNS, stated to Dr. McDONALD that the mass in the loin had practically disappeared.

The patient was rapidly putting on flesh and in every way was making marked improvement. On January 23, 1913, her father called on Dr. McDONALD in Halifax, stating that his daughter had gained 20 lbs. in weight. She ate and slept well, was up and around the house, and making steady improvement. A careful examination by two physicians in her town failed to reveal any evidence of a tumor, or mass of any kind. The toxins had been discontinued at the end of November. Dr. McDONALD states that the report of the pathologist, in his opinion, is beyond suspicion.

The patient was also examined by Dr. JOHN STEWART, one of the leading surgeons in Canada. Who confirmed the diagnosis.

Later history. — January 5, 1913, Dr. McDONALD stated :

I have just seen the father of the patient last evening : she is evidently a complete cure : weight, 136 lbs., which is her normal weight. Our pathologist, Dr. LINDSAY, an Edinburgh University graduate, who is at present on the other side, is an excellent fellow, and I have no doubt in my mind as to the correctness of the diagnosis.

June 14, 1913, Dr. BURNS, the attending physician, states :

The last injection was given on November 9, 1912 (this in spite of my advice in the latter part of January, to give her another series of injections and keep her more or less under the influence of the toxins for another six months : author). At present the patient is in fairly good health, weights 131 pounds, and advance of 32 lbs., over her weight in August, 1912 : there is not more to be felt in the abdomen by external or internal examination. She moves about freely, and has a good appetite. She has occasional stitch-like pains in the region of the scars and incision. Nothing but the toxins has wrought the change.

A letter from Dr. McDONALD this week (November 25, 1913) states she is in fine health.

NOTE. — Dr. LINDSAY on his return from Europe wrote me the specimen has not been kept but he had no doubt of the correctness of the diagnoses.

CASE 7. — *Spindle-celled sarcoma of the calf of leg; entire disappearance under twelve week's treatment with the mixed toxins.*

Case of Dr. L. L. McARTHUR (Attending Surgeon, St. Luke's Hospital, Chicago, Ill.). The patient, female, aged 40 years, entered St. Luke's

Hospital in the spring of 1894, for a removal of a tumor of the leg. Operation showed the tumor to spring from the dense fascia covering the muscles and calf. Although a very radical operation was performed, recurrence was regarded as probable, in the event of which an amputation was advised. Seven months later, September, 1894, the patient returned to the hospital with a local recurrence the size of half an egg bulging from the calf of the leg. Inasmuch as the patient was several months pregnant, it was though best to try the effects of the mixed toxins before resorting to amputation. The treatment was continued for twelve weeks with the result that the tumor entirely disappeared. Microscopic examination showed the tumor to be a spindle-celled sarcoma.

Although in April, 1896, Dr. McARTHUR wrote me that he thought there was a slight suspicion of a recurrence, this suspicion was unwarranted inasmuch as I made a personal examination of the patient in November, 1912, and found her in perfect condition, with no sign of a recurrence, eighteen years after.

CASE 8. — *Hodgkin's disease. Well five years. Advanced stage.*

This patient was treated by Dr. C. E. PRESTON of Ottawa, Can., one of my former house surgeons.

G. M., 19 years of age, was admitted to the Ottawa Hospital, May 4, 1908, with a history of glandular swelling beginning on one side of the neck and later involving both sides, of about one year's duration. There was gradual loss of weight and increasing anæmia. The glands of the neck were greatly enlarged; the spleen was enlarged and palpable three-fourths of an inch below the margin of the ribs; inguinal glands were moderately enlarged. Weight, 122 pounds. The diagnosis of Hodgkin's disease was made by all of the attending physicians and surgeons of the hospital and a hopeless prognosis was given.

The mixed toxins were begun June 1st, the initial dose being one-fourth minim. This was gradually increased until July 10th, the maximum dose of twelve minims was reached. This caused a temperature of 103°7 and a rather severe chill. The treatment was continued for about five months, partly by the family physician. Examination on January 1, 1909, showed the patient quite well, weight

145 pounds, with only a small gland in the right side of the neck. He had returned to his usual work. The toxins were discontinued.

Re-examination on September 10, 1909, by the family physician shows the patient in fine condition, all the glands have disappeared and he continues his hard work. Under date of April 6, 1911, Dr. PRESTON states he has just examined the patient and found him in perfect condition.

The patient resumed his work in a lumber camp.

Later under date of July 9, 1913, Dr. PRESTON writes :

The patient is well at present five years later.

In a letter received from Mr. ARTHUR CONNELL (University of Sheffield, England), dated July 9, 1913, he sends me the following history :

M. W., female, 37 years. Admitted to hospital January 31, 1912, discharged March 18, 1912; two children.

Four years ago first noticed a " lump " in right side; indefinite pain in right loin and semilunar line below costal margin. Feeling of constriction of waist. Occasional fainting.

October, 1910. — First noticed blood in urine on rising one morning, previous day had taken a very long walk.

August, 1911. — Second attack of blood in urine.

On these two occasions the blood quickly disappeared from urine, *i. e.* macroscopic blood.

January 31, 1912. — Admitted to the Royal Infirmary. Complained of severe pain in right loin and great desire to micturate.

In the early hours she had agonizing pain for a time which cleared up on her passing three to four long blood clots. Previously for a few days before admission had been passing very dark blood.

February 1, 1912. — R. kidney explored from behind — surface most irregular & gave the impression of polycystic disease. Deemed imprudent to perform nephrectomy, so removed a small piece for examination capsule carefully closed with catgut sutures. On February 8th, Prof. BEATTIE reported material suggested so-called Hypernephroma of kidney.

(Discharged to Convalescent House healed, March 18, 1912.)

February 15, 1912. — Second operation. *Transperitoneal Nephrectomy.*

June 12, 1912. — Returned to see me when I found her looking very ill with a huge tumor in right kidney pouch. She was readmitted forthwith and put straight way on to Coley's fluid.

October 26, 1912. — Discharged; no trace of tumor to be felt. Seen quite recently and declares she never felt better.

Extract of letter received from Mr. CONNELL, dated October 8, 1913 :

I went to the house of the hypernephroma case yesterday and thoroughly examined her and found her free from any lesion. She looks the picture of good health and declared to me, she had never felt better. She has gained weight. She works as she is widow in very poor circumstances.

CASE 9. — *Inoperable round-celled sarcoma of the upper jaw with metastases, successfully treated with the toxins by Dr. O. K. Wineberg, of Lake Park, Minn. (Published in the Medical Record of May 3, 1902.)*

A. Y., male, 41 years old. In February, 1901, was struck by the horn of a steer, causing a distinct bruise. The evidences of the latter disappeared, but at the end of three weeks he began to have pain in the superior maxilla, and a bony swelling appeared a week later on the same side. The superior maxilla was removed by Dr. WHEATON, of St Paul Minnesota, in May, 1901. The disease part could not be entirely removed, and the growth continued to increase rapidly.

His general condition was so desperate, that he was given only a few weeks to live. He wanted the toxins tried, but in view of his condition. Dr. WINEBERG at first refused; the patient insisted, however, and the treatment was started. His weight at this time was 113 pounds; he was jaundiced, cachetic, and the abdomen was markedly swollen; pulse 165, weak and irregular. At the end of three weeks' treatment the jaundice disappeared as also the metastasis in the axillary region. He had gained 11 pounds in weight, and there was marked decrease in the size of the tumor of the jaw. The toxins were given in as large doses as the patient could stand, from August, 1901, to January, 1902, 103 injections in all being given. In four weeks he resumed his work as veterinary surgeon. Four months after the treatment, he came to New York, and I presented him before

the Surgical Section of the New York Academy of Medicine. The tumor had entirely disappeared at this time. The diagnosis in this case was confirmed by microscopical examination by Prof. WILLIAM H. WELCH of John Hopkins, and Prof. JAMES EWING of Cornell Medical College. The patient remained in good health, and free from recurrence until six years later when he died of acute nephritis following alcoholic excess.

CASE OF Dr. J. C. WHITLEY (St. Louis, Mo.) :

CASE 10. — *Sarcoma of the superior maxilla.*

E. W., female; incomplete operation done in November, 1911, immediately followed by toxin treatment. The remaining portion of the tumor sloughed away and disappeared by absorption. The patient regained 30 pounds of lost weight and all symptoms of brain lesions disappeared. She received as high as 6 minims of the toxins into the tumor and 20 minims into the buttocks. I obtained a section of the original tumor, and submitted to Dr. EWING for pathological examination. His report reads :

Section show giant-celled sarcoma. Portions are made up chiefly of giant-cells, others show abundant compact spindle-cells with hyperchromatic nuclei.

Dr. EWING stated it was not a giant tumor in the sense of a myeloma, but an actual malignant tumor.

A letter received from Dr. WHITLEY, under date of July 7, 1913 stated :

Miss W. is doing fine. She has no symptoms of recurrence.

In a latter date February, 3, 1914, Dr. WHITLEY states he has just examined the patient and she is in excellent health more than two years later.

CASE 11. — *Inoperable carcinoma of uterus successfully treated with the mixed toxins by Dr. R. M. Stone, of Omaha, Neb.*

The patient, Mrs. B., aged 46 years, had lost fifteen pounds in weight; the right broad ligament was markedly infiltrated. The disease had progressed so far as to be beyond hysterectomy; three

surgeons who had seen the patient in consultation regarded the case as absolutely hopeless. The toxins were begun on December 6, 1895, and continued for two months, with the result that the tumor as well as the infiltration of the broad ligament disappeared, and the patient regained her former health. I reported the case in the *Journal of the American Medical Association*, in August, 1898. At that time, two and one-half years after treatment, the patient was perfectly well. However, three years after recovery, she developed a local recurrence which finally proved fatal. An interesting feature about this case is that though reported as a spindle-celled sarcoma, specimens of the original tumor which were sent to New York and examined by a number of the leading pathologists there, including Prof. E. K. DUNHAM and Dr. B. H. BUXTON, proved to be unquestionably epithelioma, and not sarcoma.

The disease recurred three years after disappearance under the toxins and finally caused death.

CASE 12. — *Giant-celled sarcoma of the femur, too extensive for hip-joint amputation. Entire recovery; patient well six years later.*

R. L., 19 years of age, female was admitted to the Mt. Sinai Hospital, Dr. GERSTER's service, on May 24, 1898 and remained until July 24, suffering for spontaneous fracture of the femur, from sarcoma. The diagnosis of malignancy was not made until her re-admission on December 24, 1898 when it was found that there was a shortening of $2\frac{1}{2}$ centimetres. The outer and upper aspects of the thigh were occupied by a large swelling of semi-solid consistence. There was no tenderness. The patient's general condition was only fair. On January 5, 1899, Dr. GERSTER operated, making an incision into the tumor, which latter was found to be soft and intimately connected with the bones, apparently springing from the medulla of the femur. The tumor was considered inoperable and a specimen was removed for pathological examination, and pronounced giant-celled sarcoma by Dr. MANDLEBAUM, the hospital pathologist. On January 25th the tumor was seen to have markedly increased in size and the patient was losing flesh and strength. Under my advice and direction the mixed toxins of erysipelas and bacillus prodigiosus were begun and the dose increased from 1 to 3 minims, which caused severe reaction

with chills and a temperature up to 105°. At first very little, if any improvement was noticed, the patient's general condition became greatly deteriorated and in the latter part of July, 1899 she was transferred to the Montefiore Home for Incurables. Shortly after this the tumor began to decrease in size; large masses of broken-down tumor tissue were discharged until by May, the greater part of the tumor had sloughed away and the patient began to gain a little in flesh and strength.

On May 29th, Dr. JOHN ROGESS, of New York, enlarged the opening, exposed the large bone cavity and removed considerable tumor masses by the curette, then packing the wound. On February 29, 1902 the wound was again enlarged and another curetting done by Dr. ELSBERG. The bone cavity was filled with fluid iodoform paraffin and the greater part of the wound closed. The wound rapidly healed and from this time on the patient gained rapidly in flesh and strength. Part of the tissues removed at the last operation were examined microscopically and reported as fibrous tissues, showing no sarcomatous element. By the end of the year firm union of the fragments had occurred so that the patient was able to walk without any support. She was shown before the New York Surgical Society, by Dr. ROGESS in 1903. The specimen removed by Dr. GERSTER at the original operation was examined by Prof. T. MITCHELL PRUDDEN of the College of Physical and Surgeons who pronounced it such a typical specimen of giant-celled sarcoma that he asked for some of it for class demonstration.

In this case the rapid breaking-down of the tumor, due to the toxins, followed by the absorption, undoubtedly caused the emaciation and rapid falling-off in general health. Later on, when the tumor sloughed away, the patient began to improve in general health. She was perfectly well, with entire restoration of function of the bone, six years later.

Space will not permit a full report of all the cases treated by other men. A few of the more important ones are given in full detail; the rest may be found epitomized in the following tables.

<p>9</p> <p>Dr. R. M. Stone Omaha, Neb. Medical Record, N. Y., Nov., 1935</p>	<p>Uterus inoperable very severe hemorrhages.</p>	<p>Epithelioma reported as spindle celled sarcoma. Exhaustive exam- ination proved it to be epithelioma.</p>	<p>3 months.</p>	<p>Entire disap- pearance via text.</p>	<p>Patient remained well 3 years then died of focal, recurrence.</p>
<p>10</p> <p>Czerny V. of Heidelberg, Münchener Medizinische Wochenschrift, 1935</p>	<p>Parotid.</p>	<p>Round celled size of pea.</p>	<p>18 injections.</p>	<p>Large tumor reduc- ed to small mass and removed by operation.</p>	<p>Patient alive 1 year later, and well.</p>
<p>Dr. Howard Lilienthal, New York Surgical Society Transactions Annals of Surgery and personal communication.</p>	<p>Sarcoma of ribs.</p>	<p>Round celled.</p>	<p>Mixed toxins Parke, Davis & Co.</p>	<p>Entire disappearance.</p>	<p>Patient well over 1 years</p>
<p>Dr. Chas. R. Barber, Rochester, N. Y. (personal communication).</p>	<p>Intra abdominal very extensive recurrent involving mesentery and omentum.</p>	<p>No microscopic examination but recurrent.</p>	<p>Unfiltered toxins (Burton).</p>	<p>Entire disappearance.</p>	<p>Patient alive and well Dec. 1933 18 1/2 years.</p>
<p>Dr. Horace Packard, Boston. "Five Years in Surgery" and</p>	<p>Recurrent parotid.</p>	<p>Spindle celled.</p>	<p>Toxins, unfiltered (Burton).</p>	<p>Entire disappearance.</p>	<p>Patient well 2 1/2 years later.</p>

M. Montin Maanel,
London,
Lancet, Feb. 3, 1893.

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Dr. Sydney Wilson,
N. Y. Journal of
Hypnotherapy,
Jan., 1936.

A. Marmaduke Shield,
British Medical Journal,
Jan. 23, 1897.

Dr. R. Tilly,
Chicago,
(personal communication).

Dr. J. A. Moore,
Helena, Montana
(personal communication).

Sarcoma
masloid
Goose Egg

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disappearing, & later.

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Exams, unfiltered	Exure	Patient
'Boxon'	disappearance	well 2 years later.

Entire 2 months	Well 3 months.
<p>  </p>	<p>  </p>

ur: Tumor disappeared by breaking down and sloughing. Staphylococcus infection pyemic death (toxin sterile).

Tumor disappeared.	Died suddenly 5 weeks later. Cause unknown.
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Kotire disappearance.	Patient well 2 years then local recurrence.
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Entire
artific.

Name of surgeon and reference.	No.	Sex, Age.	Date.	Locality.	Type of tumor.	Toxins, unfiltered (Burton).	Entire disappearance.	Time.
Dr. J. A. Jackson and Dr. F. L. Lewis, Transactions, Central Wisconsin Medical Society, 1907.	27	F. 36	Sept., 1936	Breast.	Clinical diagnosis confirmed by Dr. Christian Fegeer, Chicago.	Toxins, unfiltered (Burton).	Entire disappearance.	Died 1 year later with metastatic tumor in rectum.
Mr. W. H. Battle, St. Thomas Hospital, London, Lancet, April 9, 1938.	28	M. 30	June, 1937	Multiple infra supra clavicular and pectoral region and axilla.	Fibro-sarcoma spindle celled. Microscopic. Examination by Dr. Shattock.	Toxins, unfiltered 4 months.	Almost complete disappearance.	Patient shown to Medical Society of London nearly 1 year later.
Dr. T. H. Rumbold, San Francisco, (personal communication).	29	F. Adult.	Aug., 1934	Breast recurrent.	Round celled.	Toxins, unfiltered (Burton).	Entire disappearance.	Died of internal metastasis confirmed by autopsy.
Dr. H. A. Ferguson, Chicago Ill. (personal communication).	30	Adult.	1936	Sarcoma tibia.	Round celled.	Toxins, unfiltered	Entire disappearance.	Patient well 1936 10 years.
Dr. D. B. Hardenbergh, Middletown, Conn.	31	M. 46	Mar., 1937	Sarcoma iliac fossa attached to ilium.	No microscopic examination.	Toxins, unfiltered (Burton) 3 weeks.	Entire disappearance.	Patient well for 7 years when he died of other trouble.
Dr. M. L. Harris, Chicago, Ill. (personal communication).	32	F. 31	Oct., 1937	Recurrent inoperable sarcoma of ovary involving	Round celled	Toxins, unfiltered N. 1/4 to 4 in arm.	Very marked improvement tumor much smaller final sloughing of	Died 1 month later from septic absorption from sloughing mass.

Dr. F. H. Fabricius,
Greenfield, Mass.
(personal communication).

Dr. John O. Roe,
Rochester, N. Y.
(personal communication).

Radioph. Matas,
New Orleans,
and Dr. Yussell,
Philadelphia Medical
Journal, March 11, 1899,
and personal communi-
cation later.

O. K. Weinberg,
Lake Park, Minn.,
Medical Record, N. Y.

REPORT MADE BY
WILLIAM S. MILLER

Johns Hopkins,
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Cornell,

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Dr. J. C. Willy,
New Orleans, La.
(personal communication).

Mixed cells
Round and

terus

Dr. I. H. Handly,
Prof. Gynecology,
University of Maryland
(personal communication).

Dr. E. H. Robb, Newton, Ia. (personal communication).	4 times recurrent sarcoma lower jaw.	Pronounced sarcoma by Dr. Nicholas Sené, microscopic examination.	Mixed toxins (Barton).	Entire disappear- ance of tumor.	Well 8 years then metastatic tumor in foot recurred twice then disappeared with toxins. Well at present 1 years.
Dr. O. C. Davis, Augusta, Me. (personal communication).	Mixed celled sarcoma of neck recurrent large round and spindle celled.	Mixed celled large round spindle.	Mixed toxins (Barton).	Tumor $\frac{1}{4}$ size of egg involving deep structures of neck. Entire disappearance.	Patient well 4 years.
Dr. Robinson, Daus ille, Va., Personal Communication and Transaction Southern Surgical and Gynecological Associa- tion, 1914.	Round celled osteosarcoma femur.	Round celled.	Amputation for recurrence. Mixed toxins (Barton).	Entire disappearance.	Well 3 years after amputation then recurrence. Disappearance under toxins.
Ibid.	Testis operation recurred in other testis.	Round celled.	Mixed toxins.	Entire disappearance.	Well 12 years.
Ibid.	Tibia.		Mixed toxins.	Entire disappearance.	Well 5 years.
Dr. O. W. Roberts, Springfield, Mass. (personal communication).	Intra abdominal. Probably retro peritoneal size child's head.	No microscopic examination. Patient experienced much pain.	Mixed toxins, several months, Parte, Davis & Co.	Entire disappear- ance, examined by Dr. Coley, Oct., 1906.	Well October, 1913, 12 years.
Ibid.	Intra abdominal exploratory	Sarcoma, confirmed	Mixed toxins.	Entire disappearance.	Well Oct., 1915, 5 years.

Dr. R. W. Shearman,
Brooklyn, N. Y.
(personal communication).

Dr. George R. Fowler.

Dr. Howard Lilienthal,
Traverse
New York Surgical Society,
1934, and
(personal communication).

Dr. C. P. Chapin,
Buffalo, N. Y.

Dr. P. C. Roman,
Chicago, Ill.

Dr. N. S. Huntington,
Quincy, Mass.,
and J. J. Thomas
Boston Medical and Surgical
Journal, Oct. 3, 1931.

Dr. C. L. Banks,
Bridgeport, Conn.

Dr. J. Babst Blake, Boston (personal communication).	1359	Humerus involving coracoid process and glenoid cavity of scapula.	Round celled osteosarcoma.	Mixed toxins several months Parke, Davis & Co.
Dr. H. H. Beach, Boston, Mass., General Hospital case (personal communication from former House Surgeon).	59	Adult.	Ilium very large.	Mixed toxins Parke, Davis & Co.
Arthur Connel, University of Sheffield, England (personal communication).	60	June, 1912 P. 37	Kidney Hypernephroma. Large inoperable recurrent tumor June, 1912. Microscopic examination Prof. Beatle.	General condition very poor. Toxins, begun June 13, 1912. Kept up 4 months.
Sir Arbuthnot, Lase London, England (personal communication).	61	July, 1912 M. Adult.	Femur (left) near tip.	Toxins, begun Nov. 16, 1912, continued until February, 1913.
Major M. N. Bishop, N. S. A., Fort Leavenworth, Kansas (personal communication).	62	June, 1912 M. Adult.	Chest wall involving 9 th and 10 th ribs; 11 months duration, 9x9 1/2 centimetres	Disappearance of tumor. Entire disappearance. Patient well 1 year later. No recurrence.

Dr. Vradenburg (personal communication).	63	F. Adult.	July 1912	Sarcoma.	Sarcoma giant-celled microscopic examination.	Incomplete operation; much of tumor left behind toxin July, 1912.	Entire disappearance of tumor.	Patient well Jan. 1914, 1½ years.
Lilienthal, H., New York Surgical Society Reports, Feb., 1913. Annals Surg., June 1913, p. 350 (personal communication).	64	F. 20	1912	Superior maxilla.	Spindle-celled osteosarcoma.	Excision of left superior maxilla. Incomplete removal of tumor. Mixed toxins for several months.	Entire disappearance.	Well at time of last observation Jan. 1914 (9 years).
Reuven P., Little Rock, Ark. (personal communication).	65	Adult.	Feb. 1912	Femur shaft almost complete destruction of shaft.	Pathologist report Dr. A. K. McGill Little Rock, Ark. usual round-celled osteosarcoma.	Toxin, Feb. 10 July, 1913	Rapid and continuous improve- ment.	Patient well at last note less than 1 year.
Dr. Trich, President North Western Medical Society, of Ohio (personal communication).	66	M. 62	1912	Inguinal and iliac glands twice recurrent.	Lympho sarcoma round-celled.	Toxin, 3-4 months.	Gradual and complete disappearance.	Letter from Dr. Trich Jan. 29, 1914, states: Patient is in good health without recurrence more than 1½ year.
Dr. F. Mikula, Cincinnati, Ohio (personal communication).	67	F. Adult.	Aug., 1912	Ovary involving horn of uterus and sigmoid.	Sarcoma exploratory op. microscopic examination.	Toxin, sept. 1911, until June 1912; dose M. 1 to M. 21	Immediate relief of pain and decrease in size of tumor.	Entire disappearance of large inoperable umor in 6 months

single large retro-peritoneal cyst; no other recurrences.

Patient well
Nov., 18, 1912,
5 years later.

sarcoma
very malignant
character -
called.
knee

Landing Smith, Rockside
d, Denmark
(personal communication).

Dr. G. reporter
patient well,
May, 1910, well
April, 1911,
3 1/2 years
Oct., 2, 1913,
6 years later has
local recurrence.

Sarcoma
inoperable
sarcoma
un.

Dr. M. B. Gowland,
Milton, Ont., Canada
(personal communication).

Patient in good
health
4 years later,

Ovary inoperable
Sarcoma
regarded hopeless.

Dr. F. L. Toser,
Washburn, Me.
Vermont, Med. Monthly
(personal communication).

Patient well last
observation,
4 years later,

Patient well last
observation
4 years later.

Sarcoma clinical
diagnosis only.

Ibid.

Ibid.

Patient in good
health with no trace
of recurrence
3 years later.

Sarcoma clinical
diagnosis.
Recurrence in
inguinal and
iliac region
3 months after
removal of testis.

Dr. Percy Shields,
of Cincinnati, Ohio.
(personal communication).

Dr. Miketa and Dr. Oliver
(personal communication)
and Surg. Gyn. Dept.,
Aug. 1911.

Prinos C. E.
Ottawa, Canada
(personal communication).

Massachusetts General
Hospital.
Records courtesy of
Dr. Harner
(personal communication).

Massachusetts General
Hospital.
Records of Dr. Harner
(personal communication).

girdle in neck

Sarcoma
Sarcoma
teeth and

pathologist at
Massachusetts
General

Sarcoma nose
and med. Dr

Massachusetts General
Hospital.
Records courtesy of
Dr. J. W. Harner, of Boston.

Massachusetts General
Hospital.
Records courtesy of
Dr. Harner, physician.

Massachusetts General
Hospital.
Records courtesy of
Dr. Harner.

Critic, Dr. Geo. W. and
Drs. McWhorter and Stanton,
and Ober,
Surg. Gen. and Obst.
Aug. 11, 1911.

Three operation last, incomplete toxins.	Toxins begun 1 week after operation and continued 3 weeks M ₁₄ to M ₁₆ .	Patient reported well 1 year later, without recurrence.
Tumor alone excised testis left.	Put on toxins, 1 month later kept up for 3 weeks.	Patient in good health now 3½ years later.
		No evidence of recurrence 2 months later.
		Toxins showed less and less effect. Rapid growth. Death Feb. 1, 1912, complete autopsy no metastases.

Name of surgeon and reference.	No.	Sex. Age.	Locality.	Type of tumor.	Treatment duration.	Result immediate.
Dr. Percy Shields, Cincinnati, O.			Right iliac fossa near medial head.	Sarcoma clinical diagnosis not confirmed by microscopic examination.	Exploratory incision showed tumor springing from ilium toxas begun kept up 3 months M. 4 to M. 10.	Entire disappearance of tumor in 3 months.
Dr. M. Barry, Whitaville, Mass., and Dr. E. G. Brackett (personal communication).			Sarcoma sternum and ribs recurrent.	Sarcoma microscopic examination and X-ray examination.	First operation Jan., 1918. July, 1919 large local recurrence called inoperative by Dr. Brackett, of Boston.	Toxins begun July 7, continued 7 months in injections. Complete recovery disappearance of tumor.
Dr. J. C. Whaley, St. Louis, Mo. (personal communication).			Sarcoma superior maxilla involving frontal sinuses and ethmoid.	Sarcoma spindle and giant celled. Dr. Ewing said it was not a true giant celled sarcoma but a real	Incomplete operation much of tumor left behind toxins begun at once; rest of tumor sloughed out and disappeared by absorption.	Toxins: local M. 6 and systemic up to M. 21. Patient gained 25 lbs. in weight and symptoms of brain pressure disappeared.
Dr. A. L. Smith, New Brunswick (personal communication).					Exploratory operation Dr. Robert Abbe, St. Lukes Hospital, April, 1916.	Steady increase in size July, 1919, filled nearly whole right half abdomen.

No.	Sex. Age.	Date.		Treatment duration.	Result immediate	Result
91	M. Adult.	1916	Orbit recurrent from retina.	Melanotic sarcoma microscopic exami- nation. Boston City Hospital, 1914.	Incomplete operation, Nov. 21, 1916; Toxins, 3 months.	3 1/2 years later had metastases in liver, and died June, 1916.
	F. child.		Intra abdominal involving aescu- lary infestines	Sarcoma inoperable microscopic examination.	Exploratory laparotomy; ite- garded as hopeless.	Well 1 1/2 years later.
	F. 41		Left ovary recurrent in pelvis inoperable.	Round celled sarcoma.	Toxins, 2 months.	Patient remained well for 4 years then had another recurrence same region, no longer controlled by toxins.
	Kidd, Dr. Frank, London, England (personal communication).		Ramus of lower jaw perosteal.	Small spindle celled sarcoma no giant cells.	First operation February 25, 1909, removal of R. ramus recurred July '11. Second operation followed by toxins	Toxins continued Letter Sept. 22, 1912, Dr. Kidd states: "There is no sign of recurrence; patient 4 years well."
			Sarcoma abdominal wall inoperable.	Spindle celled sarcoma microscopic examination.	Exploratory op. Sept. 5, 1916, toxins begun Sept. 22, 1916. Part toxins prepar- ation; of Cady's toxins.	End of 1 month no improvement general condition worse. Toxins left off; 2 months later, Local and general improvement. Toxins resumed continued 3 months.
	Major C. G. Spencer, Royal Army Med. Corps, Trans. Royal Soc. Med. London, 1919.					Entire disappear- ance of tumor. Letter from Major Spencer June 27, 1913 states: "Patient was well when last heard from a year ago. Well for 6 years."

Paul M. Fieber,
Brooklyn
personal communication.

Sarcina of
wall
Round celled

months.

Mrs. Thompson and Gruter,
Surg. Gyn. and Obst.,
Aug., 1911
(Coley).

improvement

Dr. David S. Kennedy,
Appleton, Wis.
personal communication.

Dr. Wm. Dietz,
Spokane, Washington
personal communication.

Dr. Deaneley,
Brit. Med. Jour.,
May, 28, 1910
and personal communication.

113	Dr. J. H. Gibbon, Jefferson Hospital, Philadelphia, Surg. Gyn. and Obstetrics, Aug., 1911. and personal communication.	Sarcoma. Spindle celled.	Amputation reduced excision; local recurrence 3 wks later. tumor began at base.	Tumor pushed to severe reactions X rays used at same time. Entire disappearance.
114	Dr. Geo. H. Keller Philadelphia, University Pa. Hosp. Francist. Philadelphia Med. Society Annals of Surgery, Feb. 1912.	Lympho sarcoma neck recurrent in	Lympho sarcoma microscopic examination by pathologist of University Hosp.	Tumor, no other Complete recovery, treatment.
115	Dr. Arthur B. White, Haver, N. Y. (personal communication).	Ovary mesenteric testes.		
116	Dr. W. D. Haines, Cincinnati, Ohio (personal communication).	well inoperable.		
117	Dr. W. D. Haines, Cincinnati, Ohio (personal communication).	Sarcoma		

Dr. A. L. Smith,
New Brunswick
(personal communication).

William C. M.,
Grand Forks, N. D.,
reported in full
Surg. Gyn. Observers,
Aug., 1911 (Coley).

M. E. Green
(personal communication),
Amer. Journ. of Obstet.,
Dec., 1917.

Ibid.

Ibid.

Tumor removed together with outer table of skull. Prompt recur. Hopeless prognosis given.	Tumor began. Entire disappearance of tumor.	Well at present 5 years.
Toxist April 22 August, 1906.	Complete recovery without sacrifice of limb.	Patient well more than 4 years later.
	Entire disappearance no trace of tumor since 1917.	No recurrence and patient in good health

Kansas City (personal communication).		microscopic examination.			over 3 years.
Ibid.	Neck inoperable.	Sarcoma microscopic examination.	Toxins.	Recovery.	Well over 3 years.
Ibid.	Humerus inoperable (without amputation).	Sarcoma microscopic examination.	Toxins.	Recovery.	Well over 3 years.
Ibid.	Neck.	Sarcoma microscopic examination.	Toxins.	Recovery.	Well over 3 years.
Legueux.	Recurrent after removal of both breasts.	Carcinoma.	Toxins 5 months.	Entire disappearance at end of one month.	Patient well Dec., 1913, 6 years.
Ibid.	Recurrent local, with enormous oedema of arm.	Carcinoma.	Toxins several months.	Disappearance of tumor.	Patient well more than 3 years later.
Dr. H. H. Greenwood, Leeds, England, Lancet, Janv., 19, 1912 (personal communication).	Neck recurrence.	Sarcoma melanotic microscopic examination.	Incomplete operation, rapid recurrence, toxins begun March, 3, 1911.	Improvement immediate, entire disappearance by July, 1911, injections continued 2 years and 1 month.	Total number of injections = 15; highest dose = M. 15, patient in splendid health July 1913 over 2 years.
Dr. H. H. Mac Donald, Halifax, N. S., and Dr. A. S. Burns of Kentville, N. S. (personal communication).	Kidney involving retroperitoneal glands.	Exploratory laparotomy inoperable microscopic examination small round celled sarcoma.	Patient much emaciated and regarded as quite hopeless, toxins begun, Sept., 1912.	Toxins given for 3 months, entire disappearance, gain 22 lbs. in weight.	Patient in good health one year later.

Well at present.

Dr. John Morley, surgeon,
Manchester Hospital,
Manchester, England,
lecturer clinical anatomy
Manchester University
(personal communication).

Patient well,
16 years later.

W. L. Robson,
Prof. surgery
medico-surgical College,
Philadelphia
(personal communication).

Patient well,
Aug. 1910,
4 years later.

Sarcoma

Dr. Louis Bocker,
Pensacola, Fla.
(personal communication).

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